

FIG. 1A

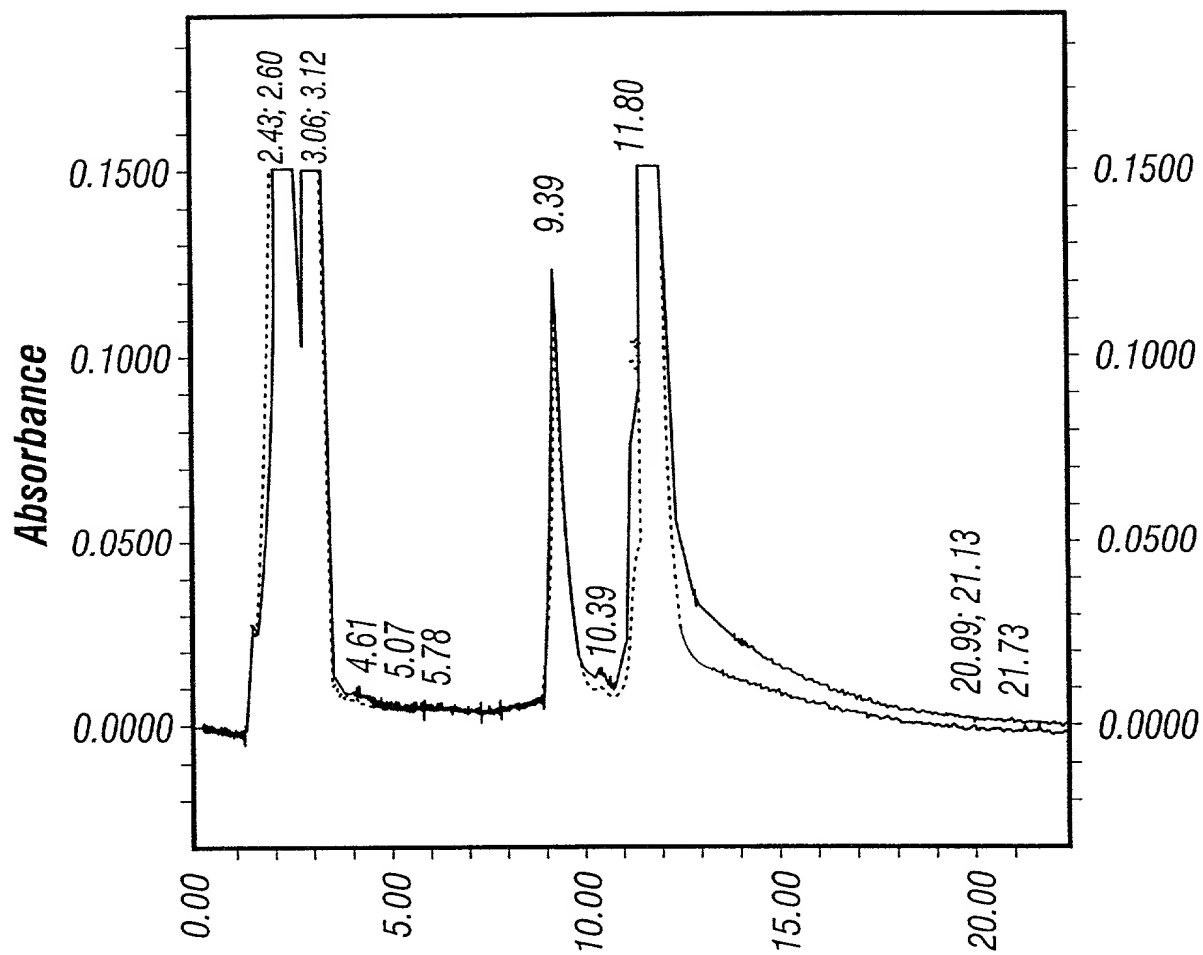


FIG. 1B

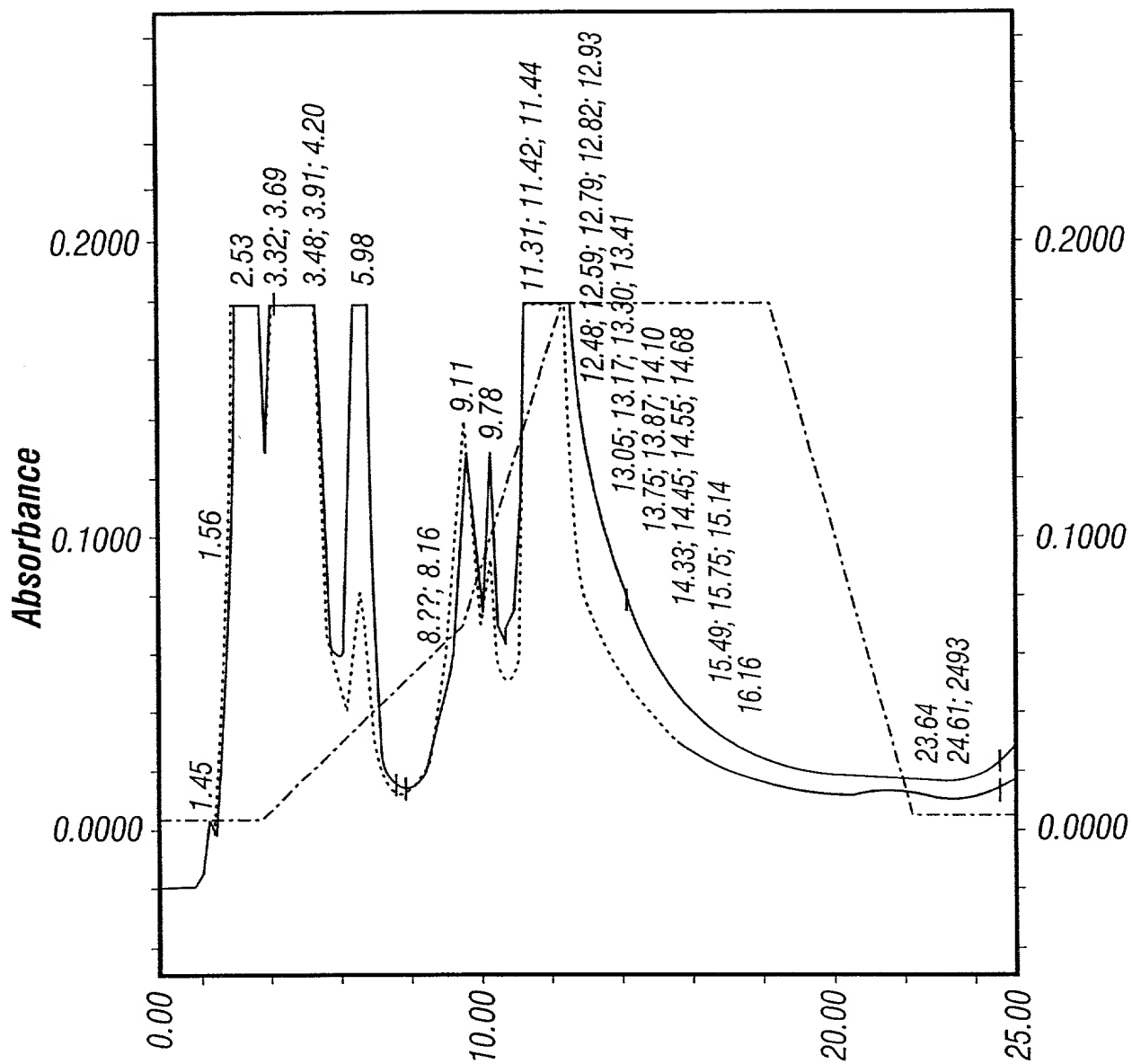
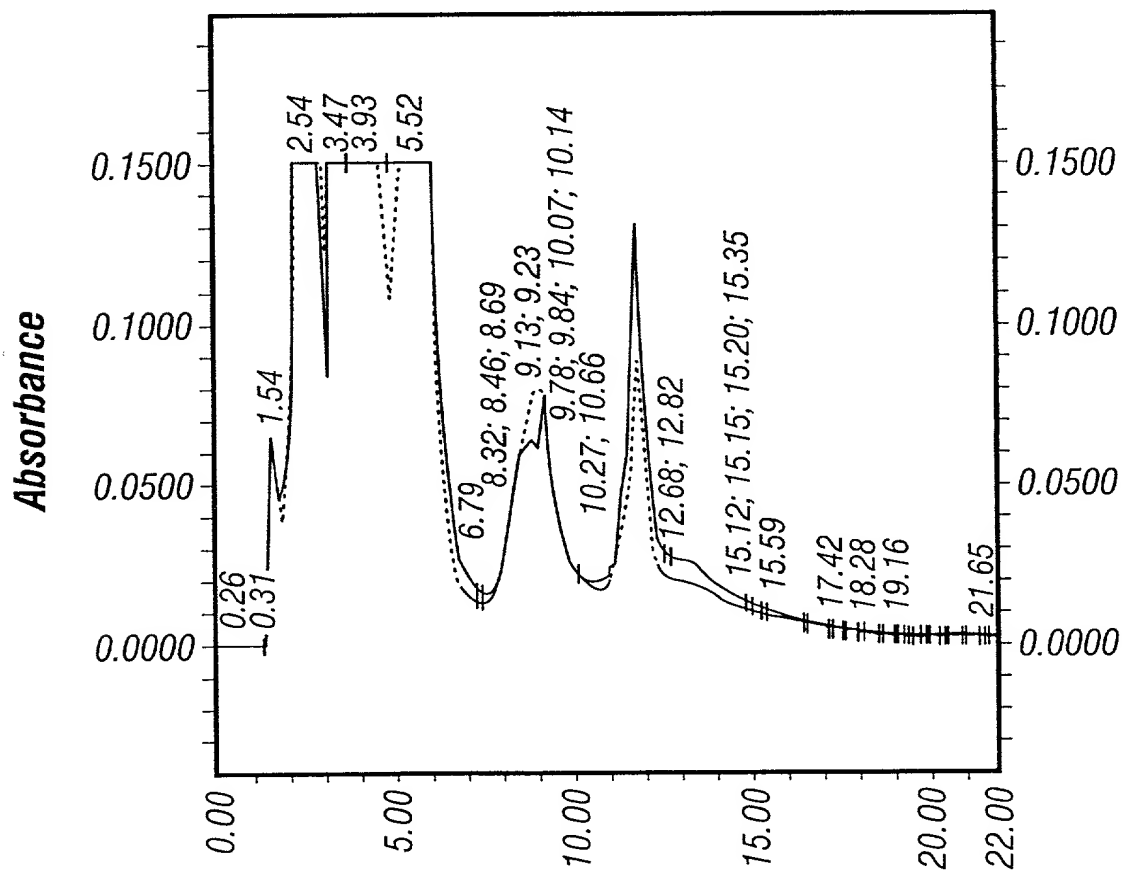
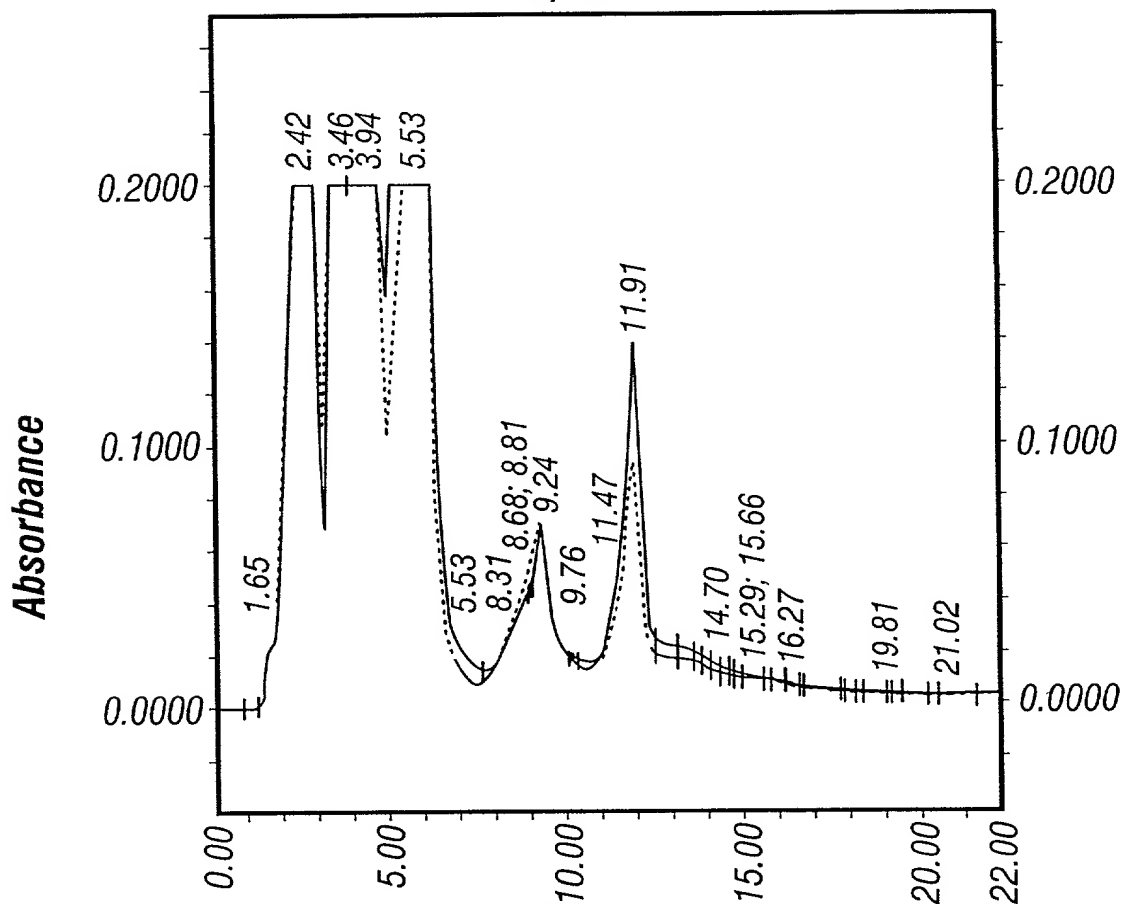


FIG. 2

4/48



4/48

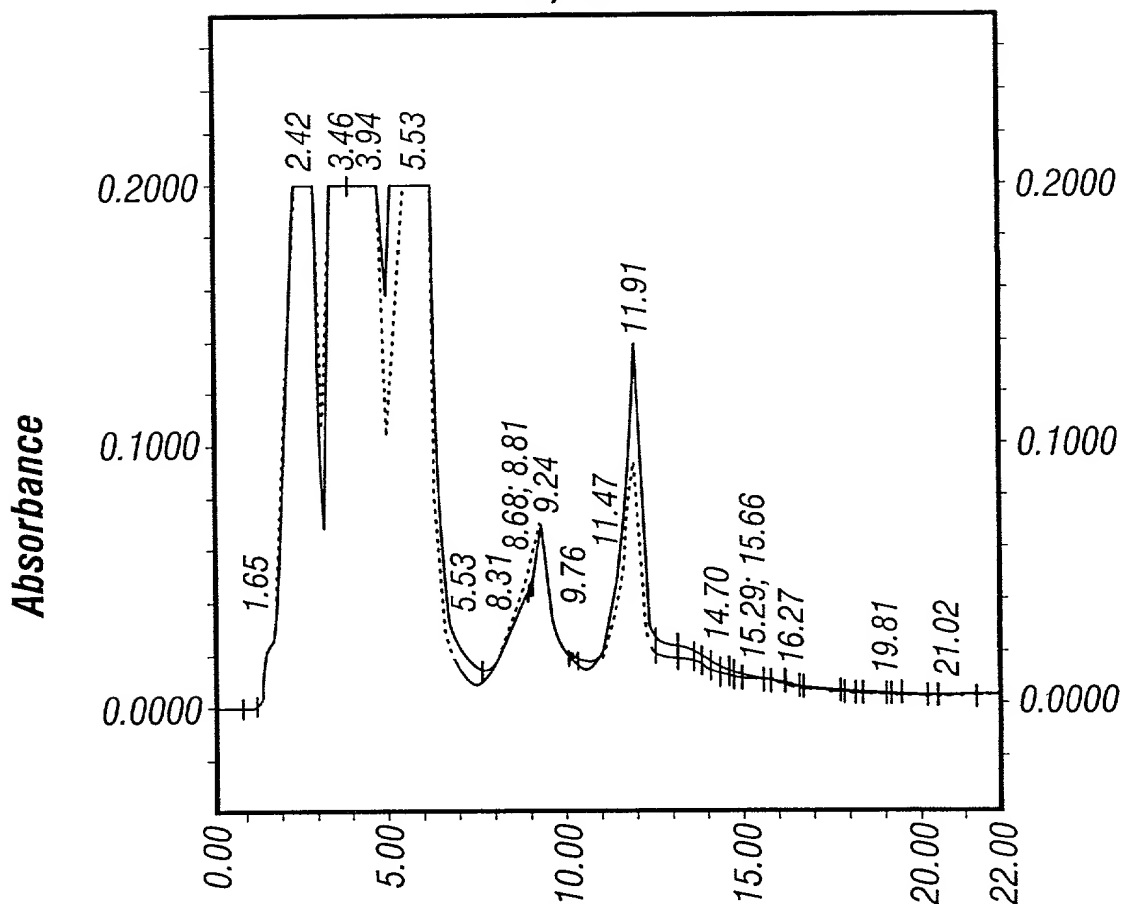


FIG. 3A

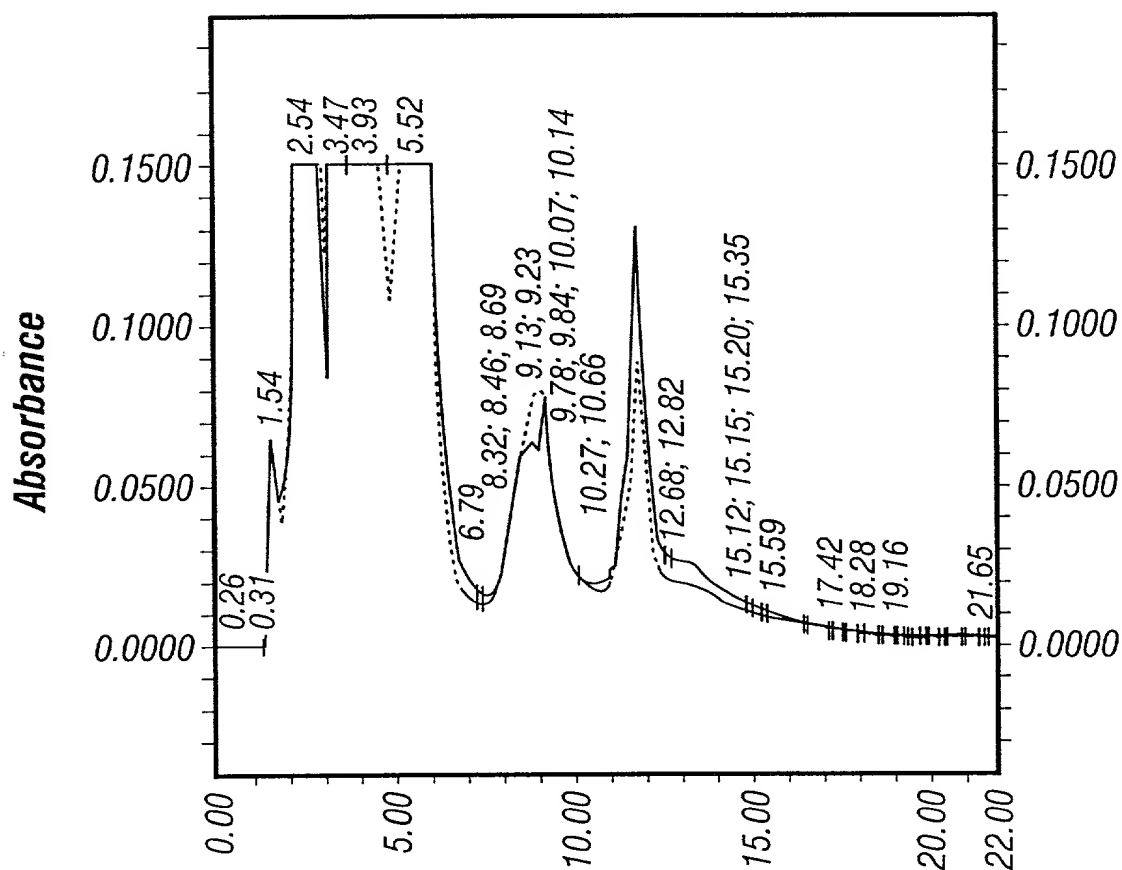


FIG. 3B

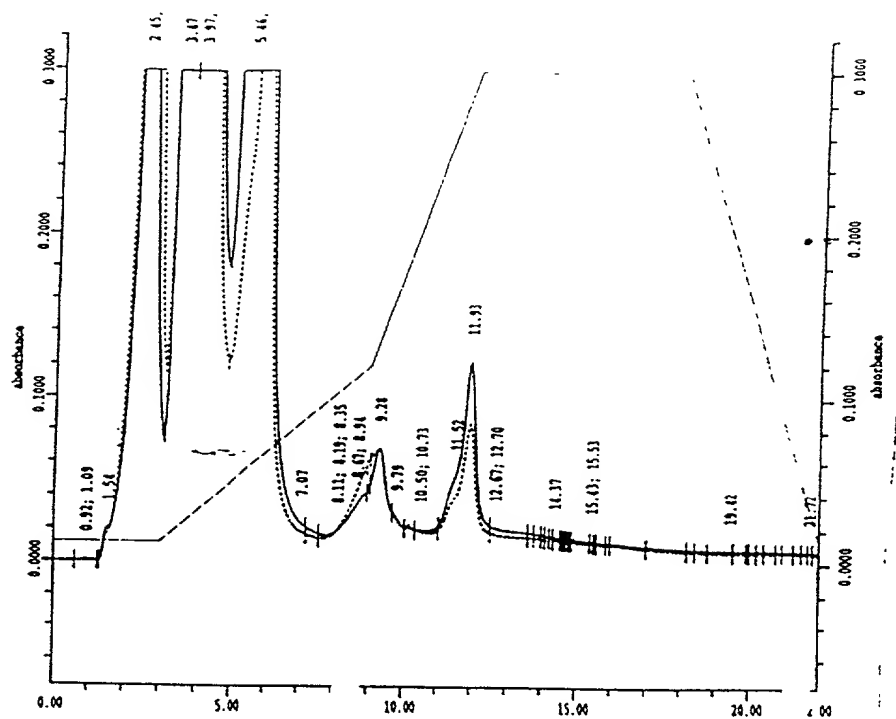


FIG.3C

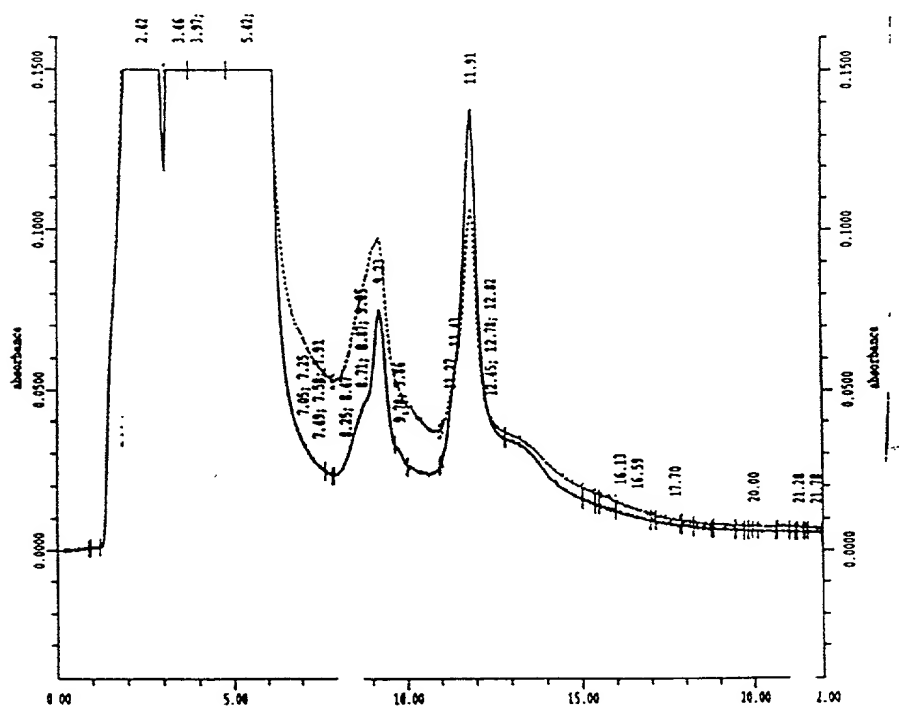


FIG.3D

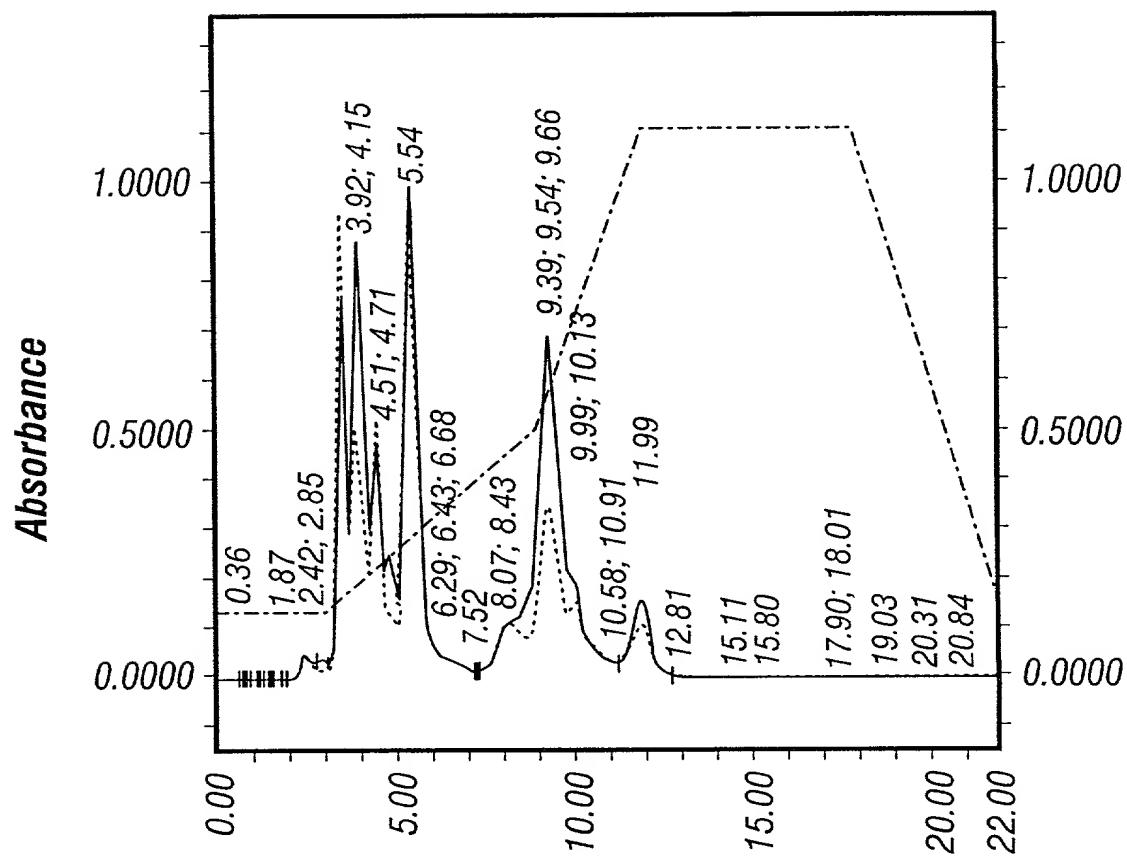
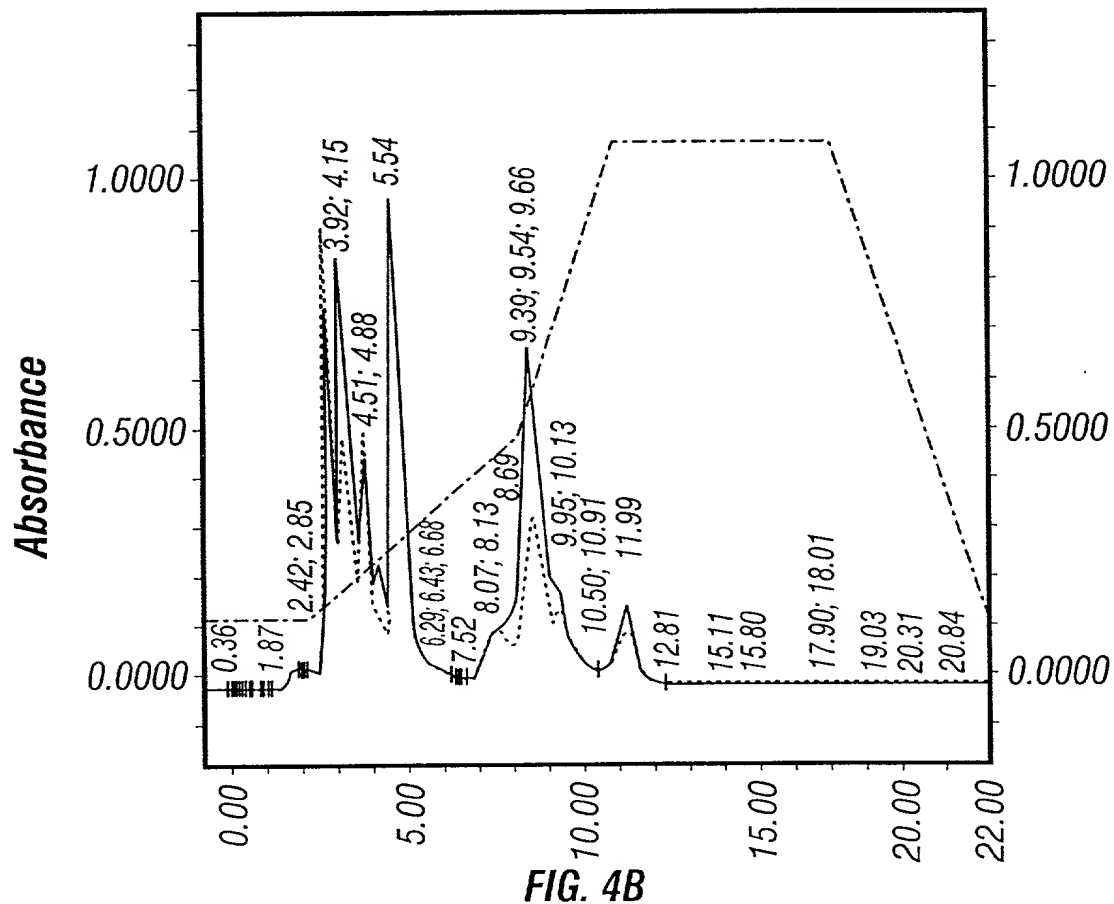
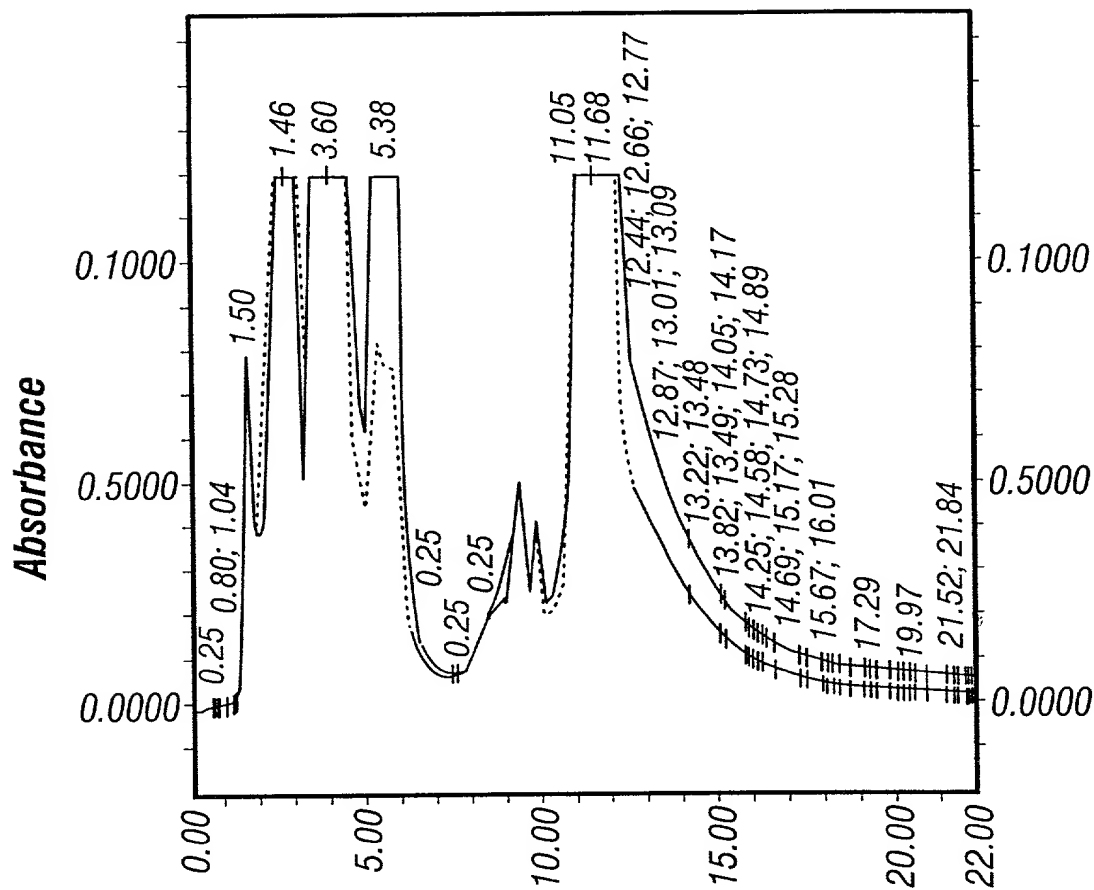


FIG. 3E





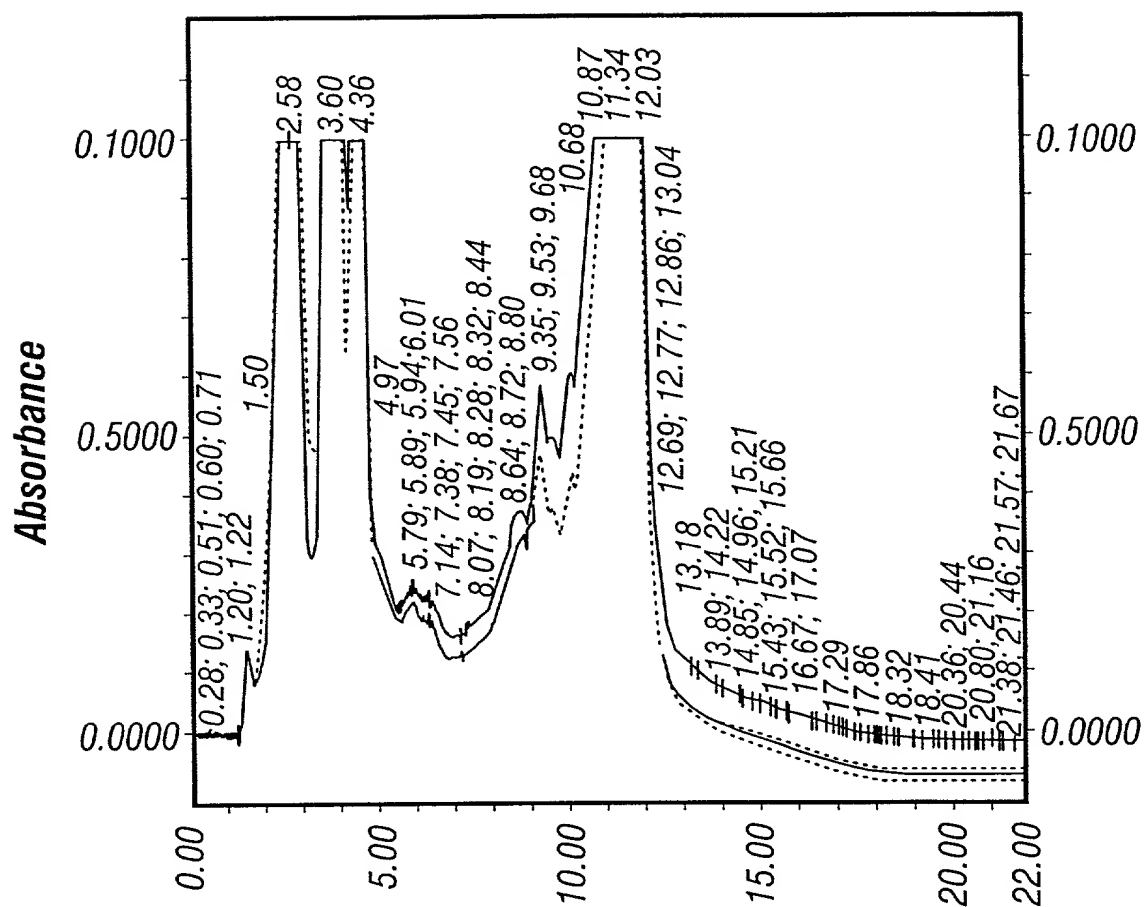


FIG. 5

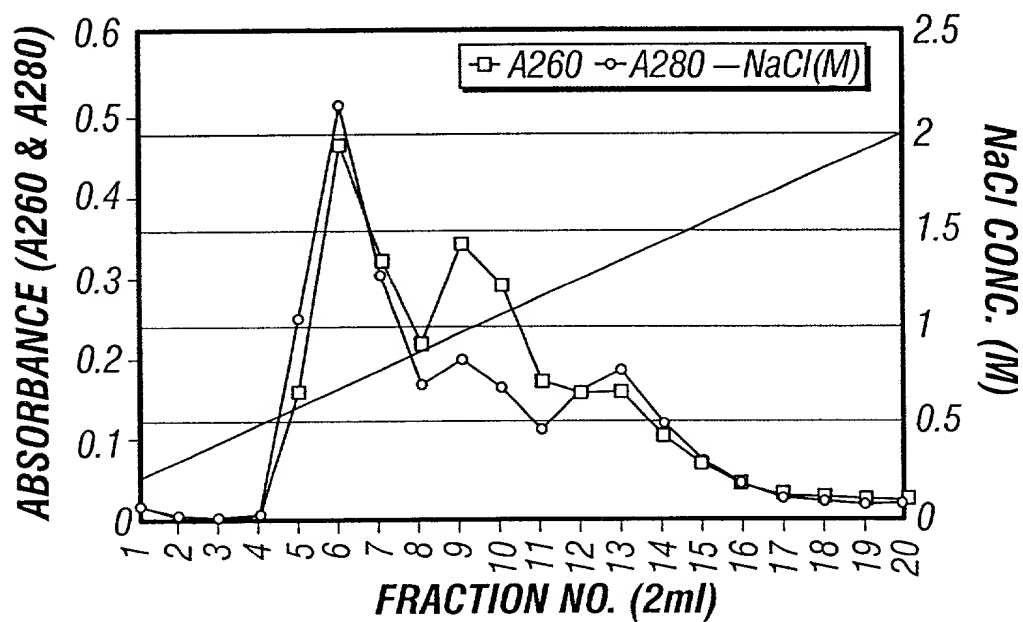


FIG. 6

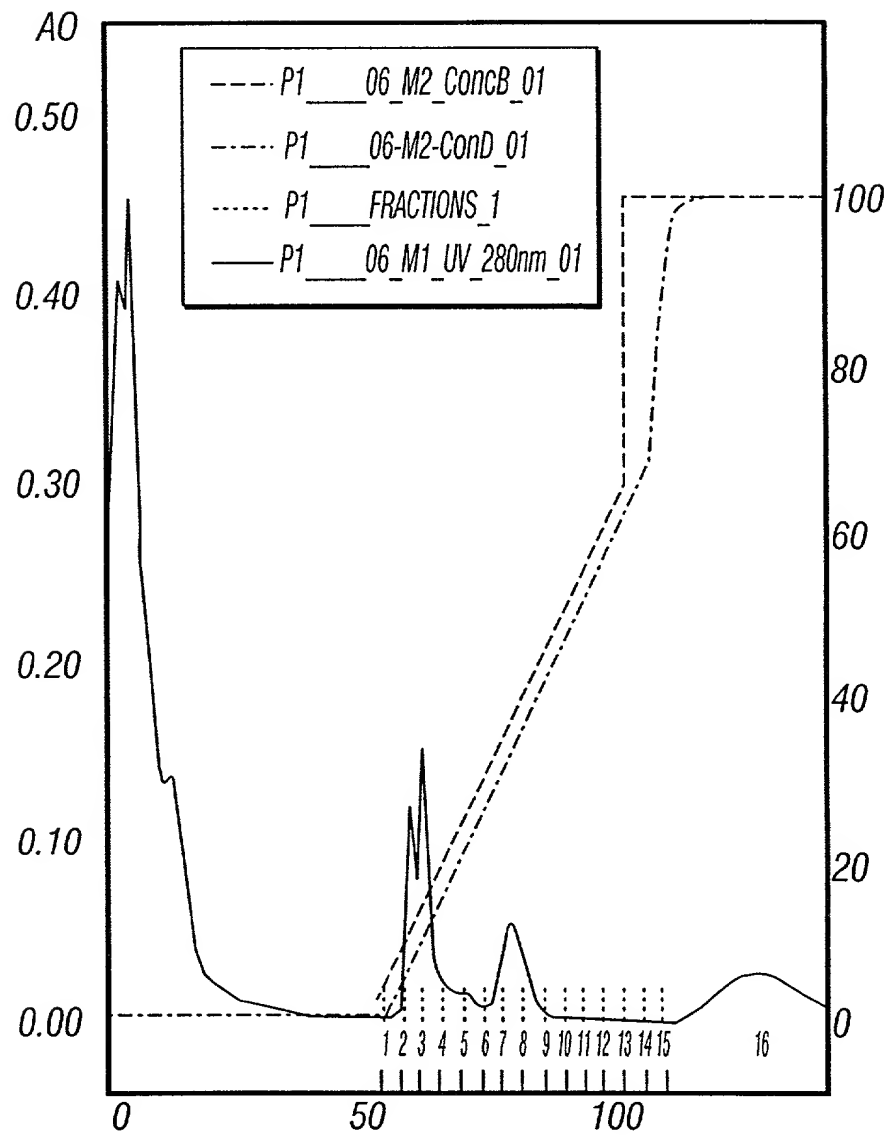


FIG. 7

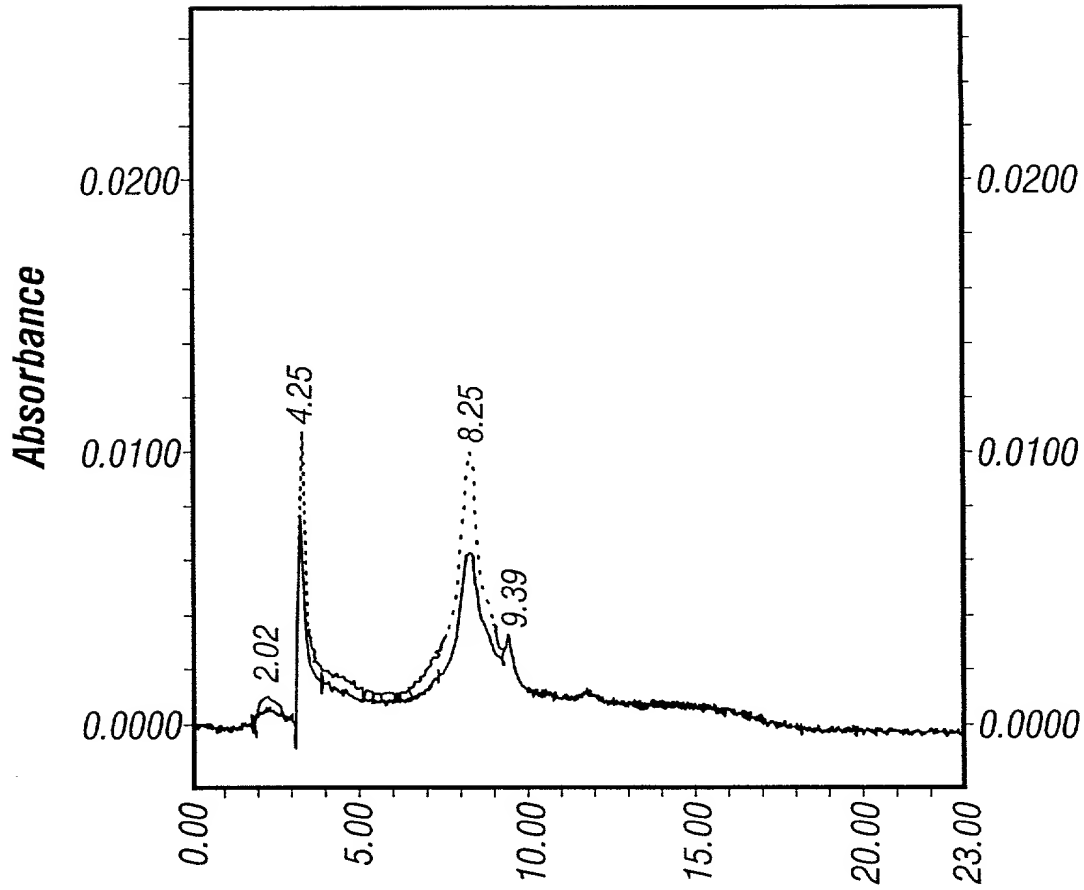


FIG. 8A

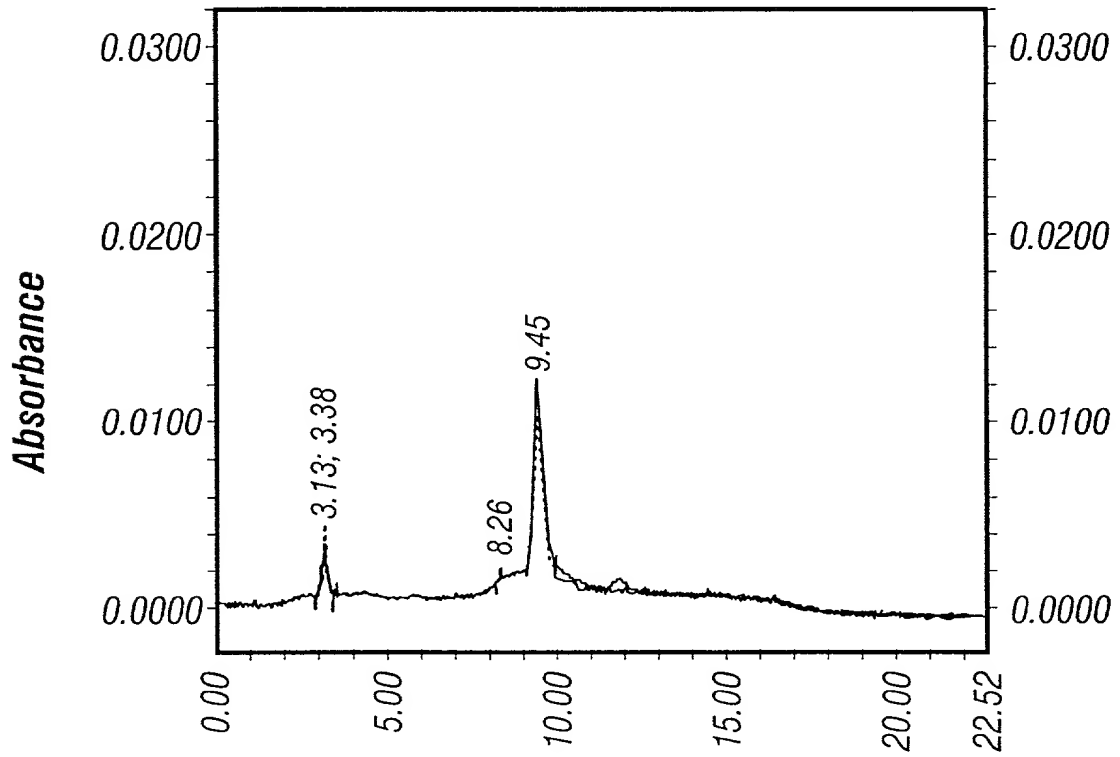


FIG. 8B

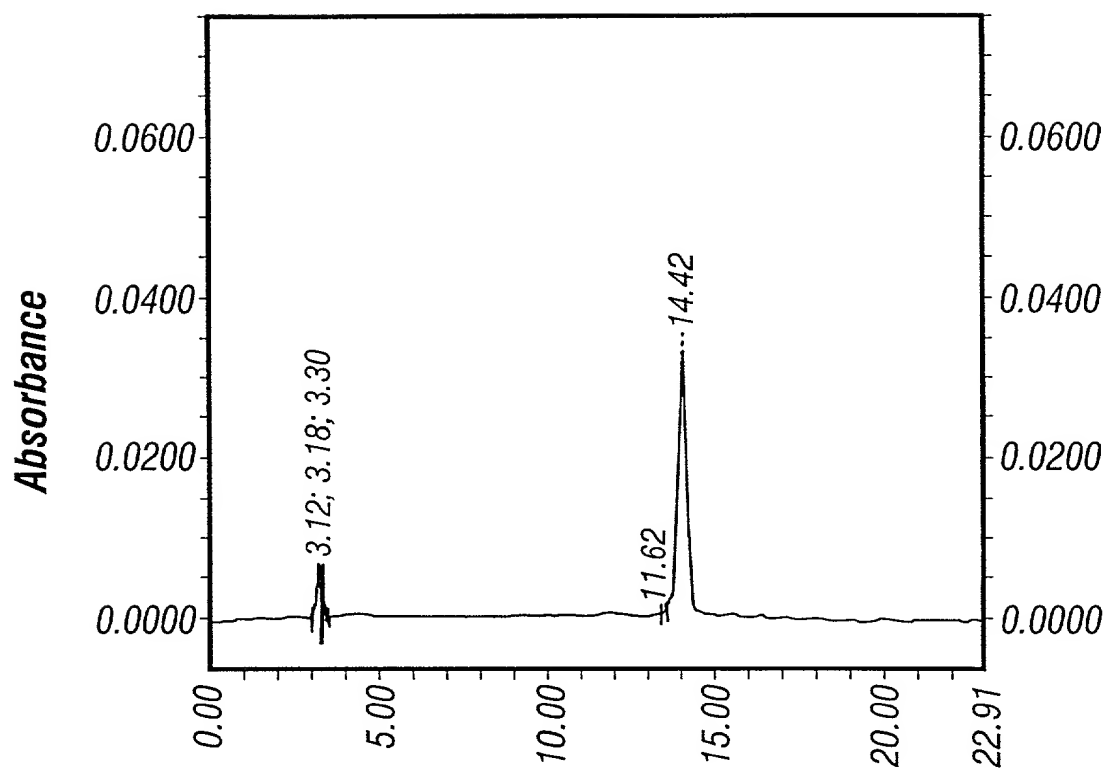


FIG. 8C

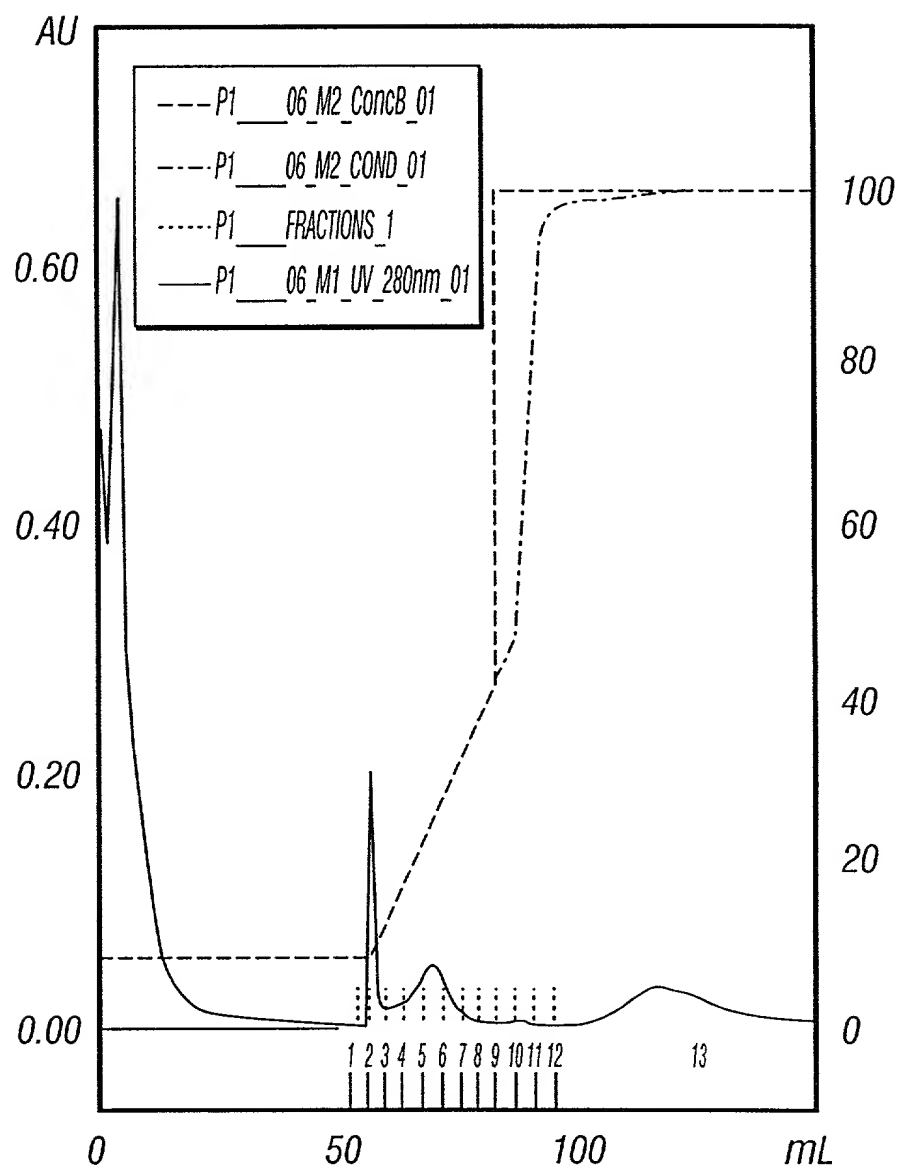


FIG. 9

12/48

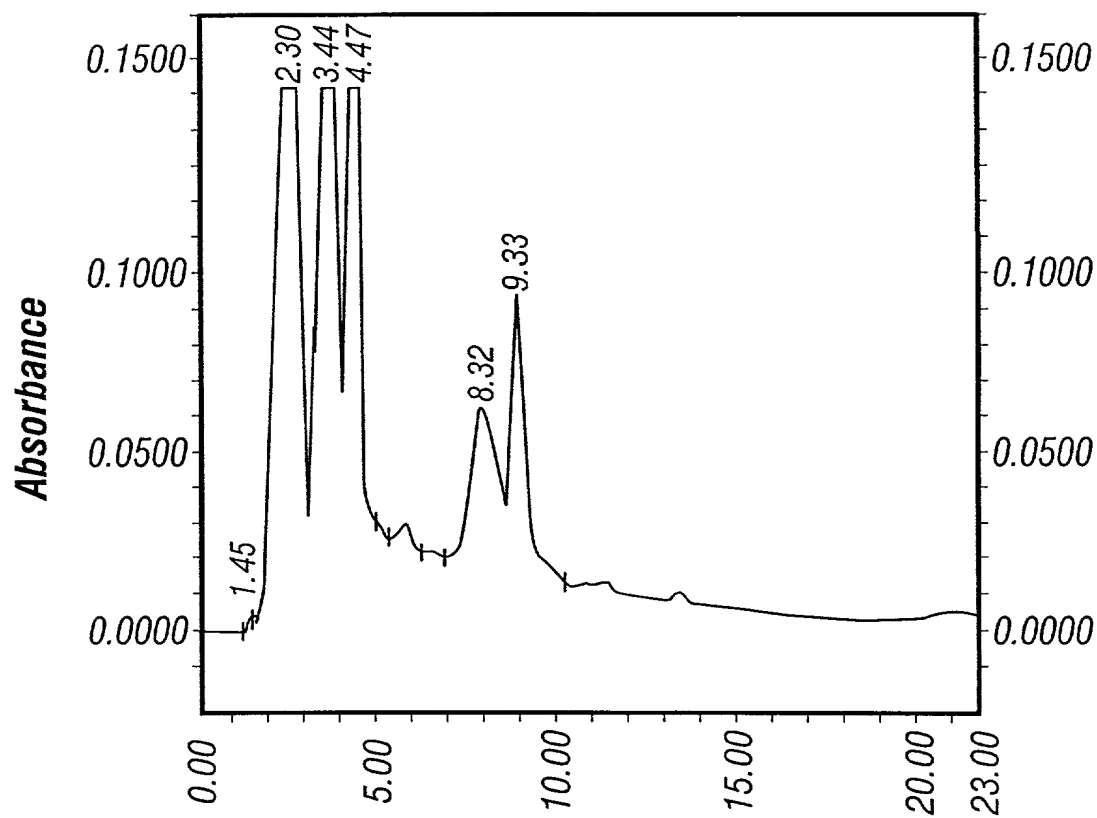


FIG. 10A

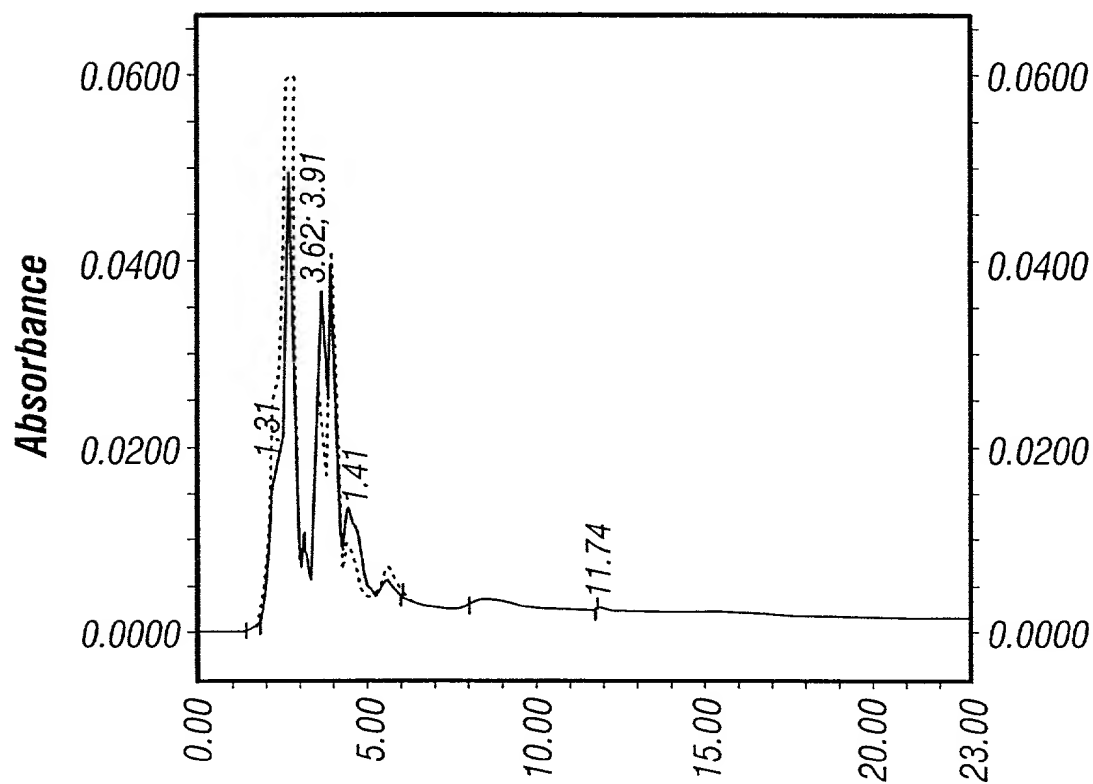


FIG. 10B

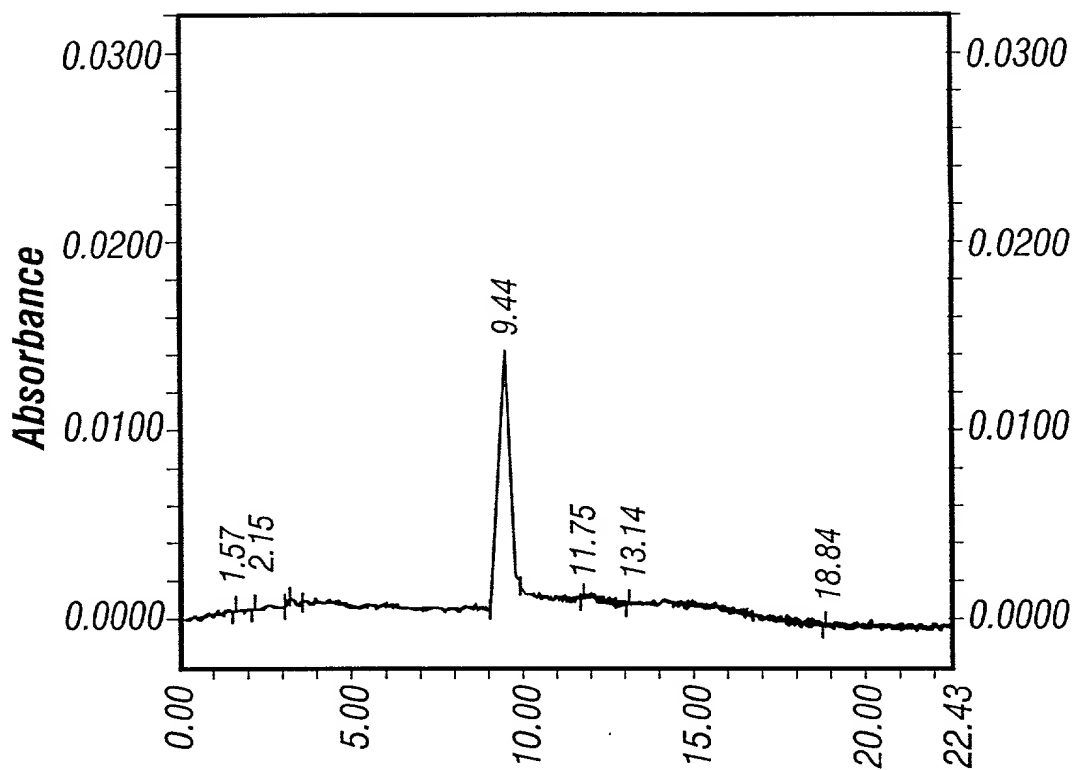


FIG. 10C

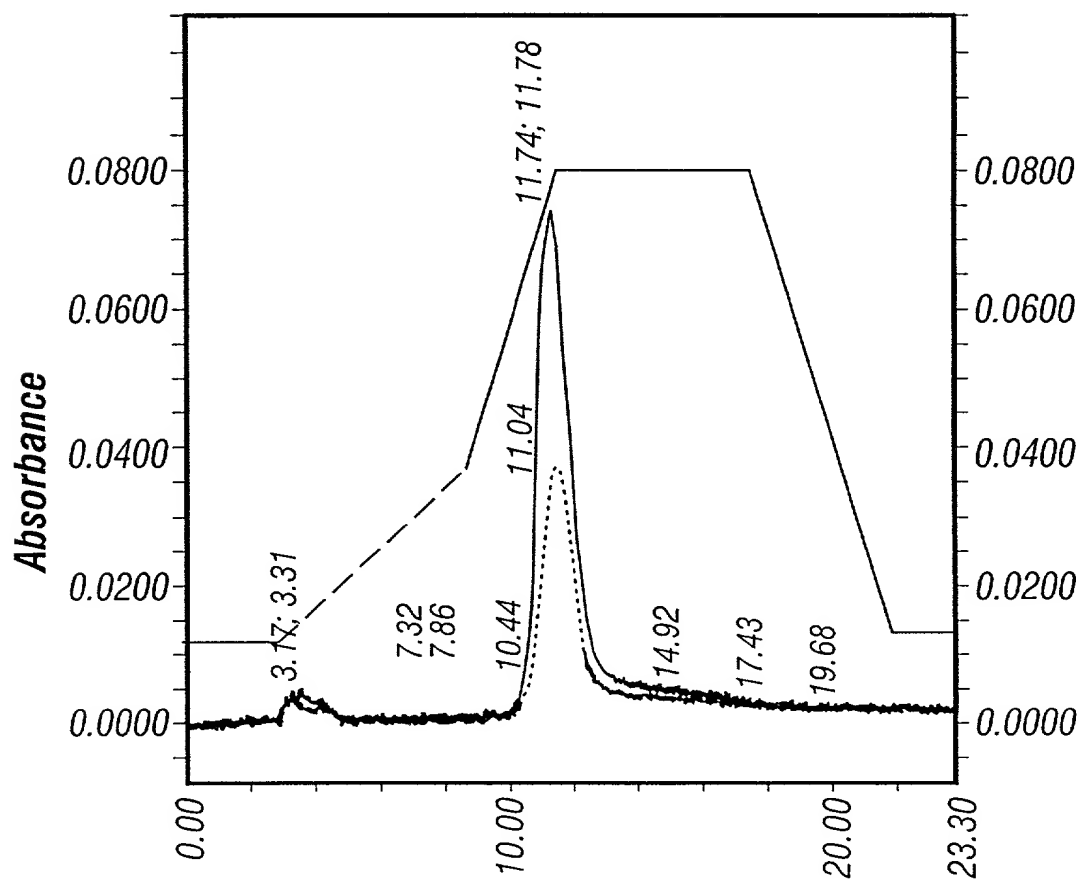


FIG. 10D

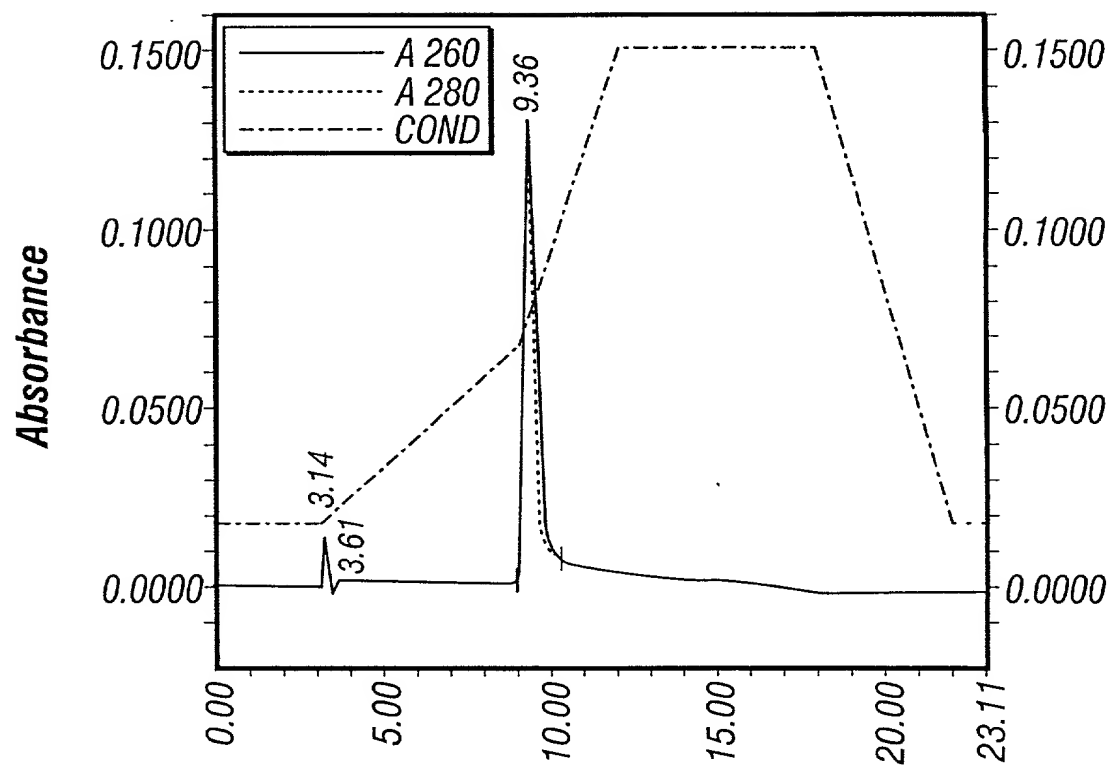


FIG. 10E



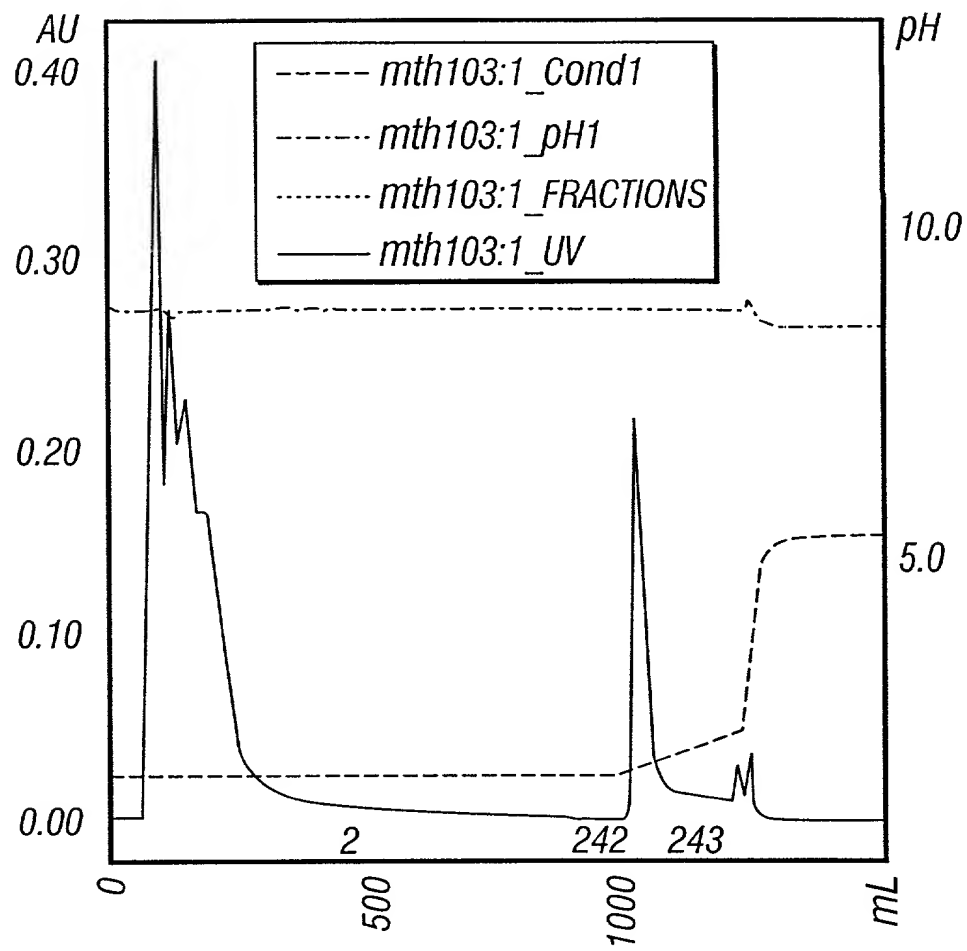


FIG. 11

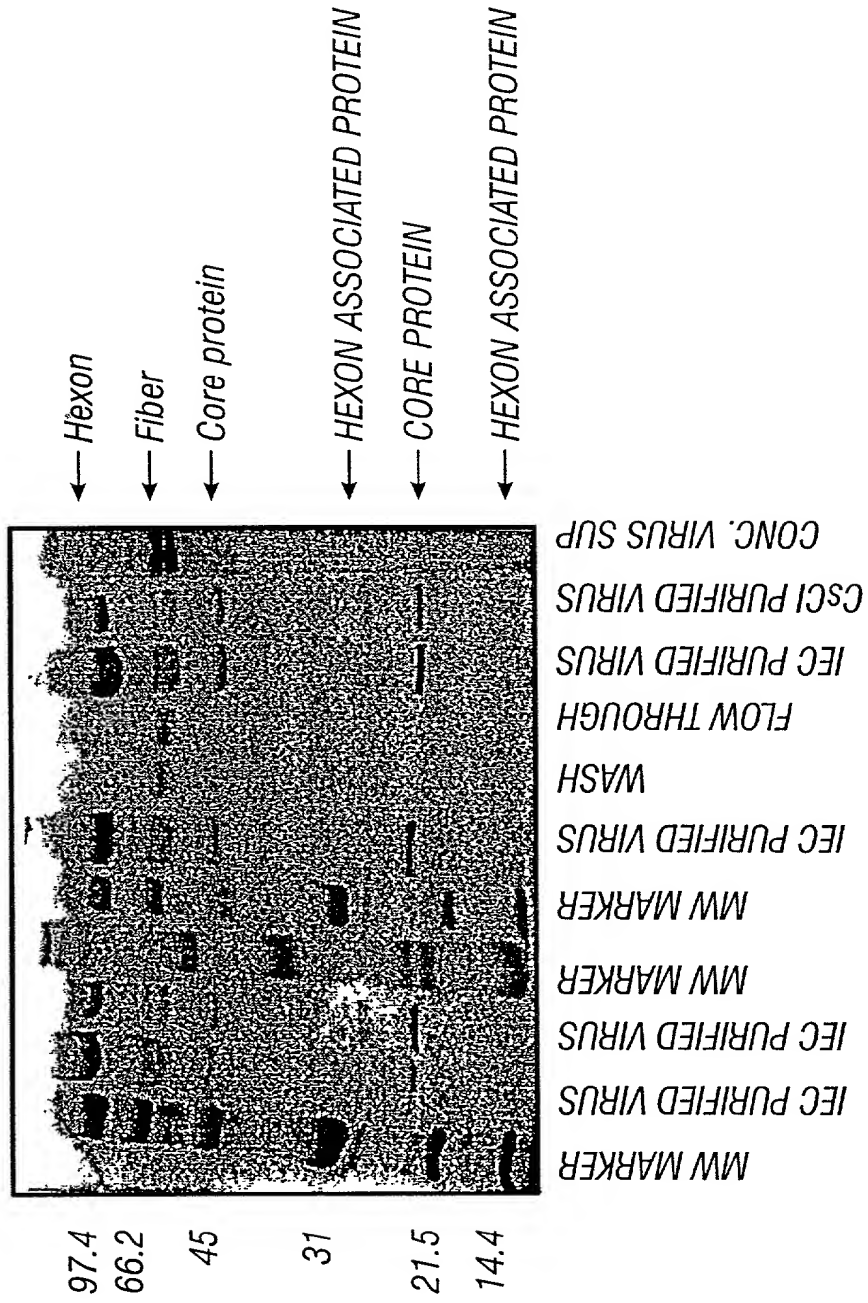
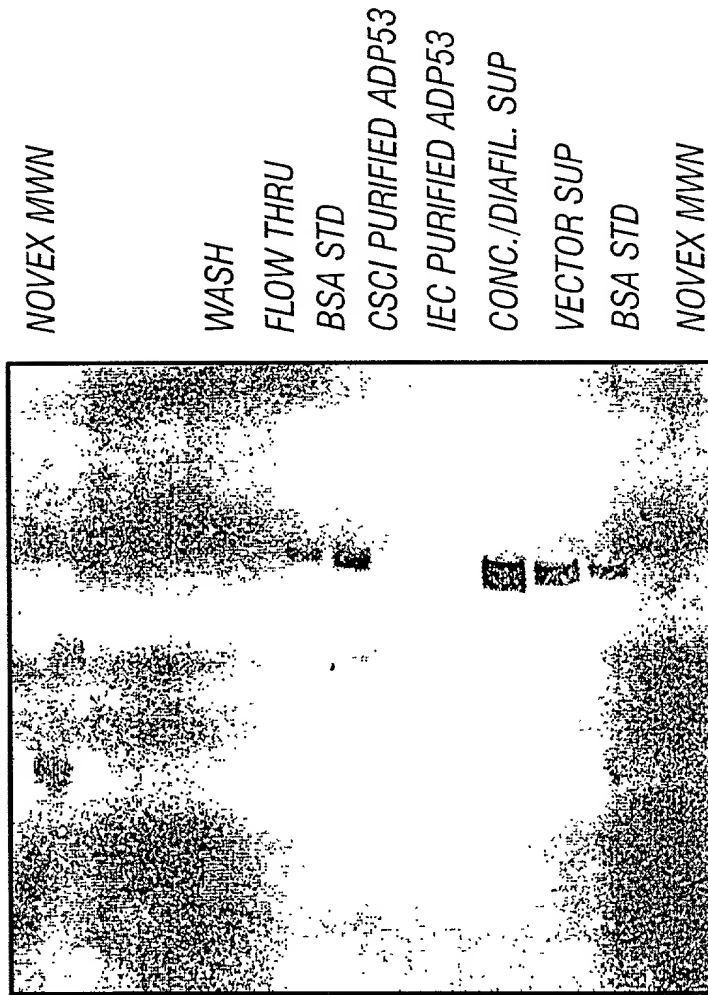


FIG. 12



66.2KD

FIG. 13

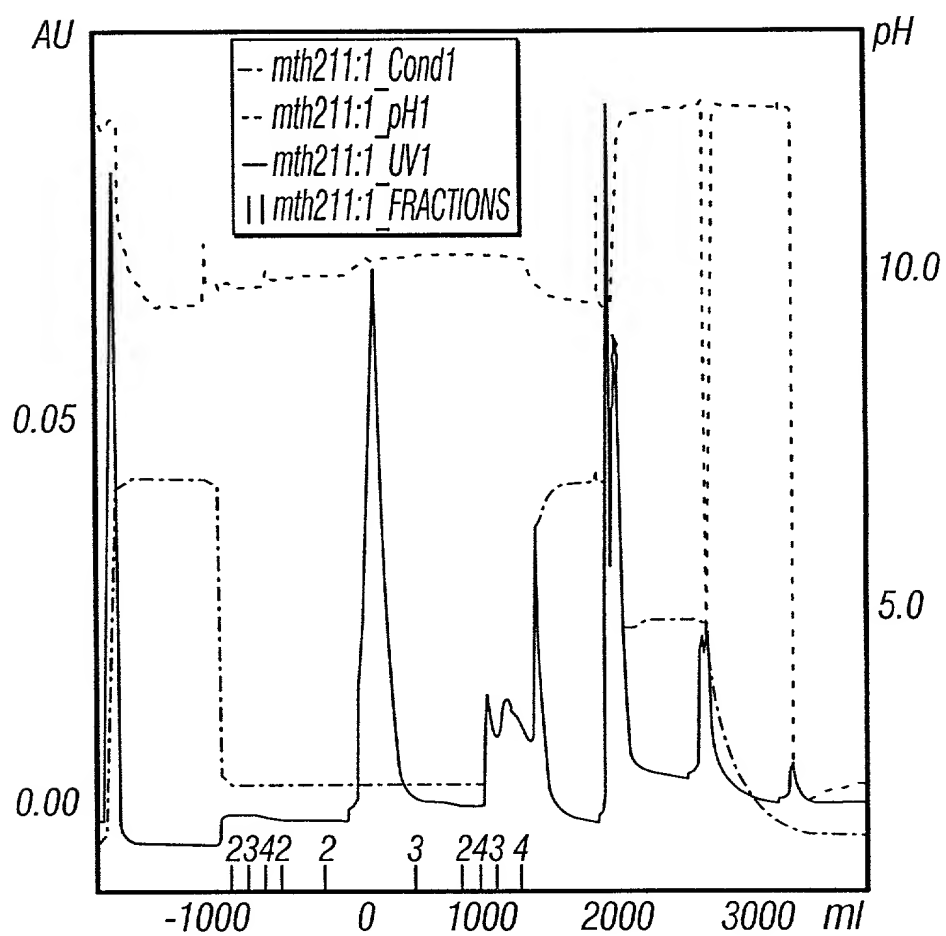


FIG. 14

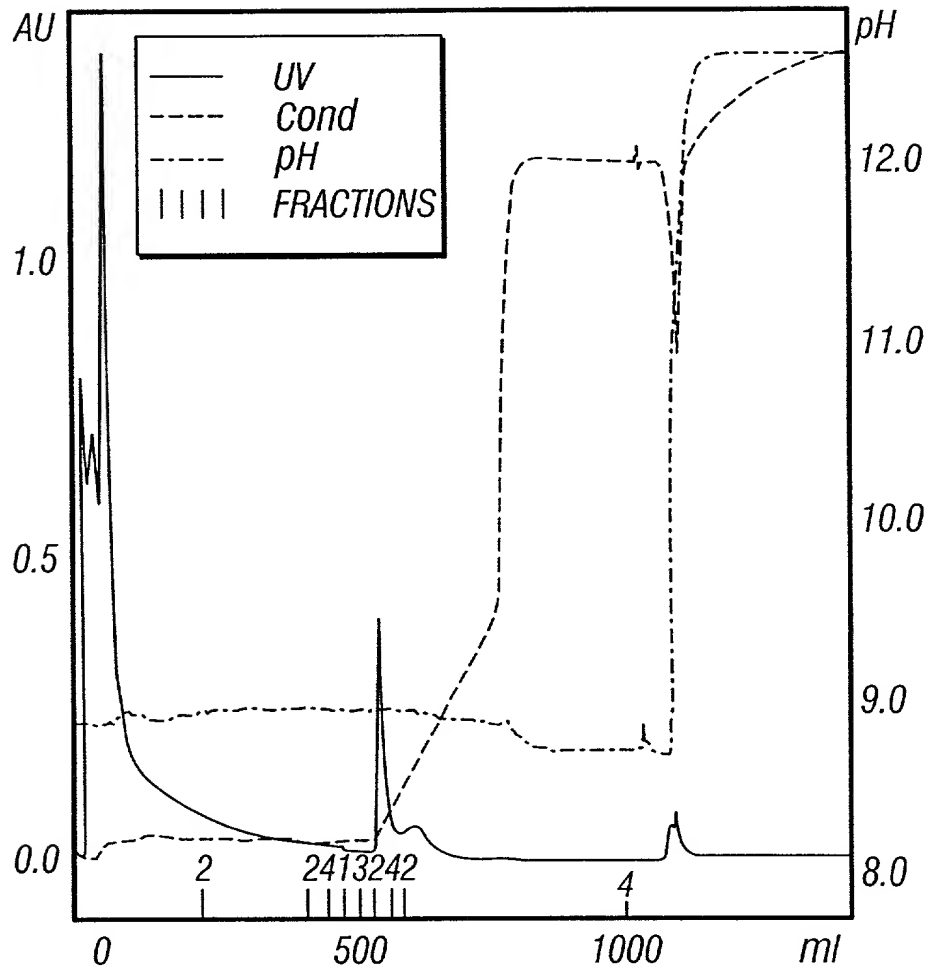


FIG. 15

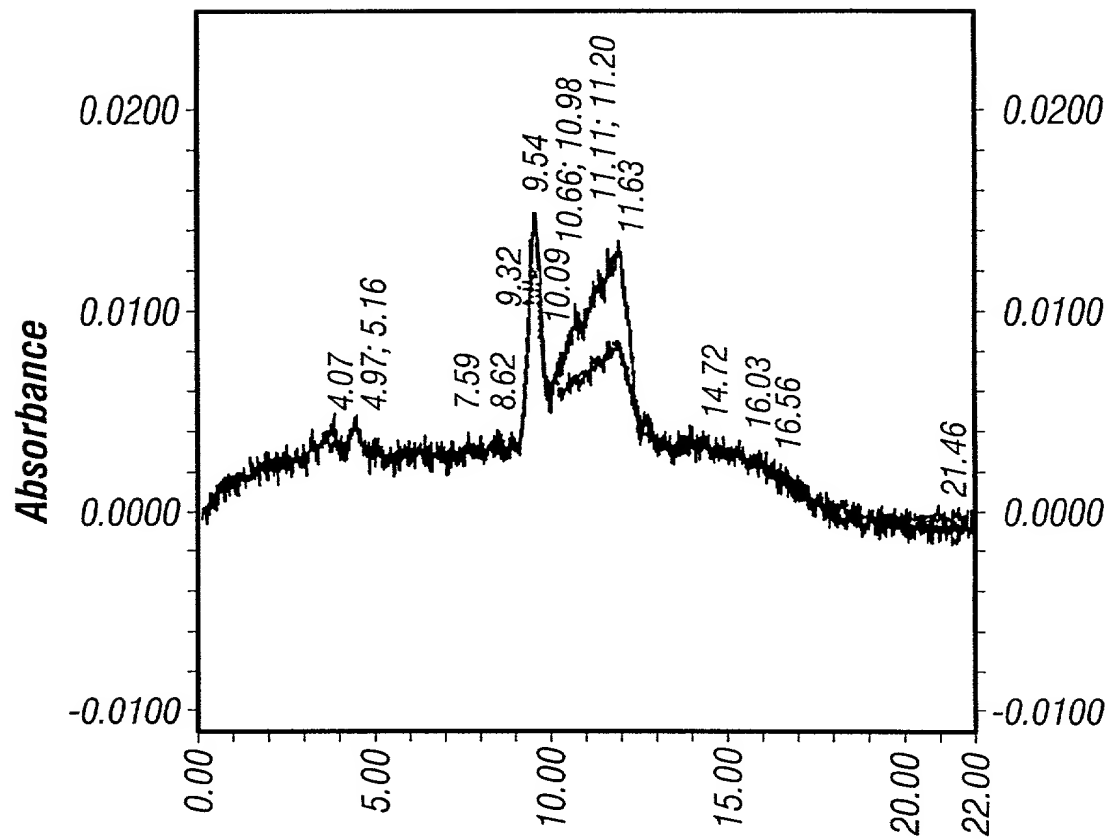


FIG. 16A

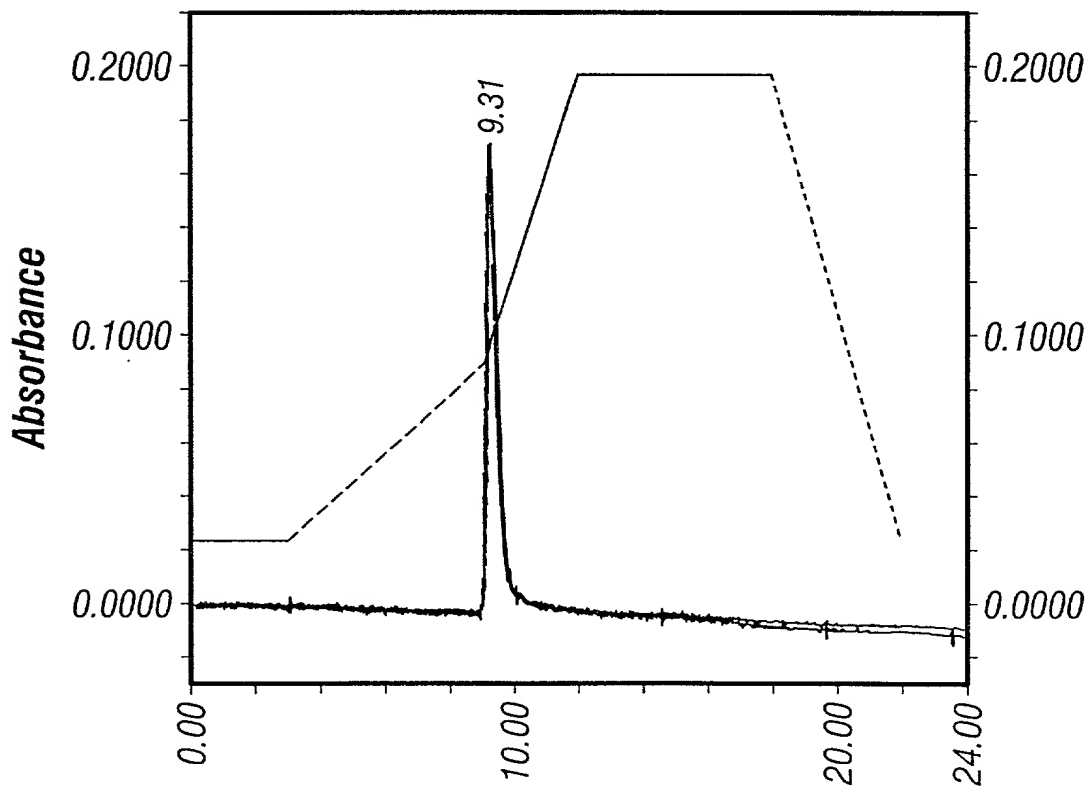


FIG. 16B

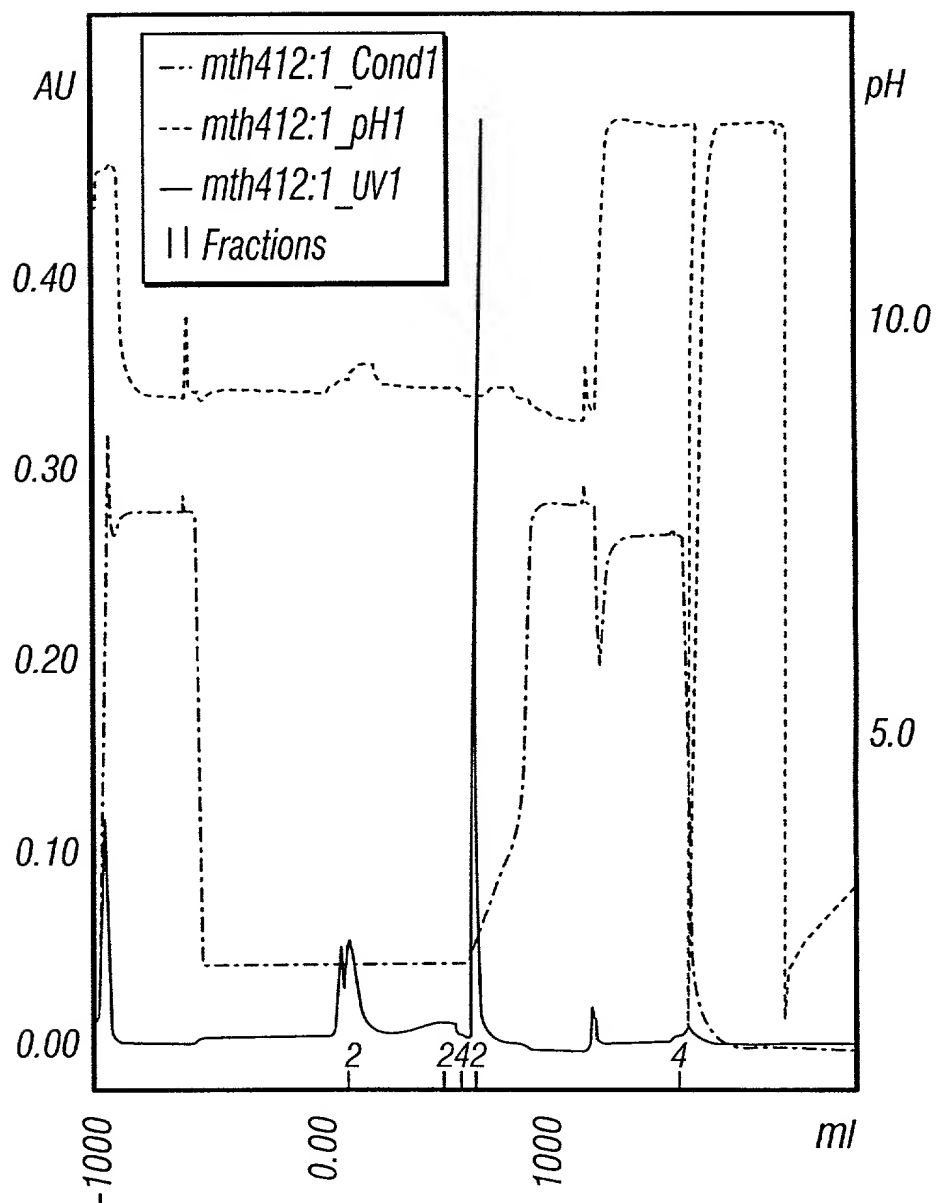


FIG. 17

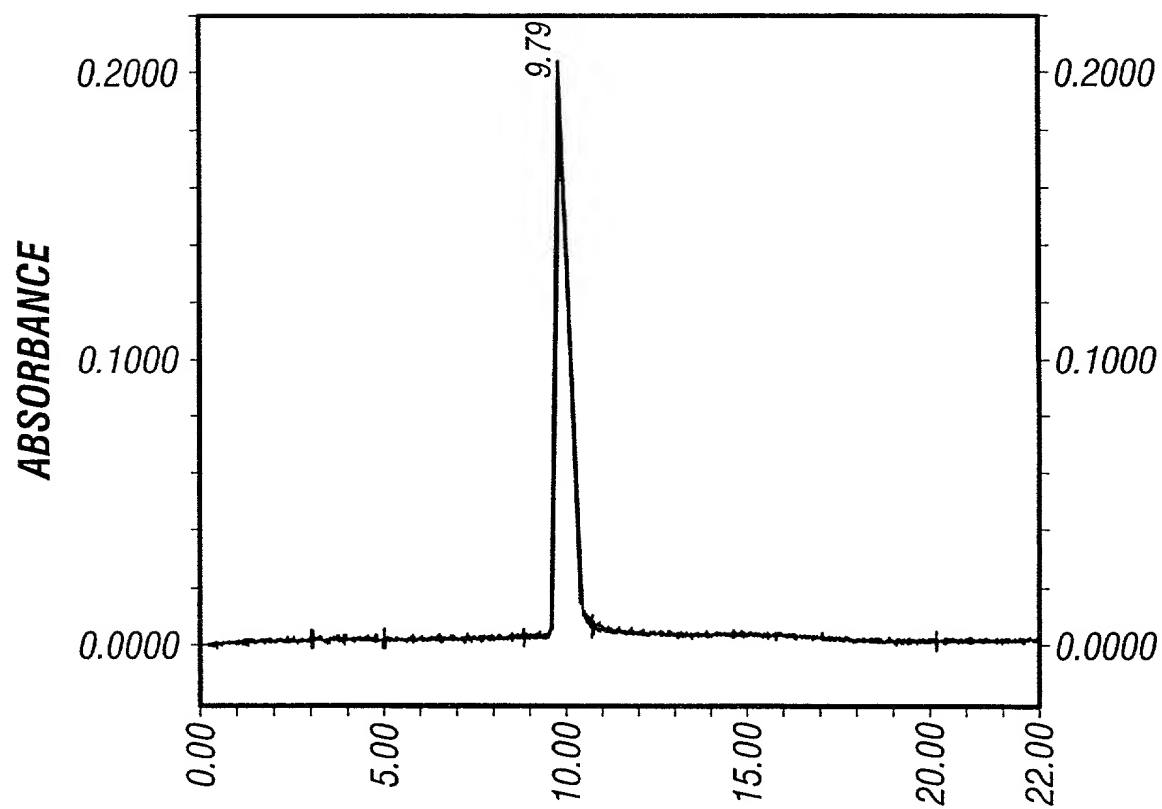


FIG. 18



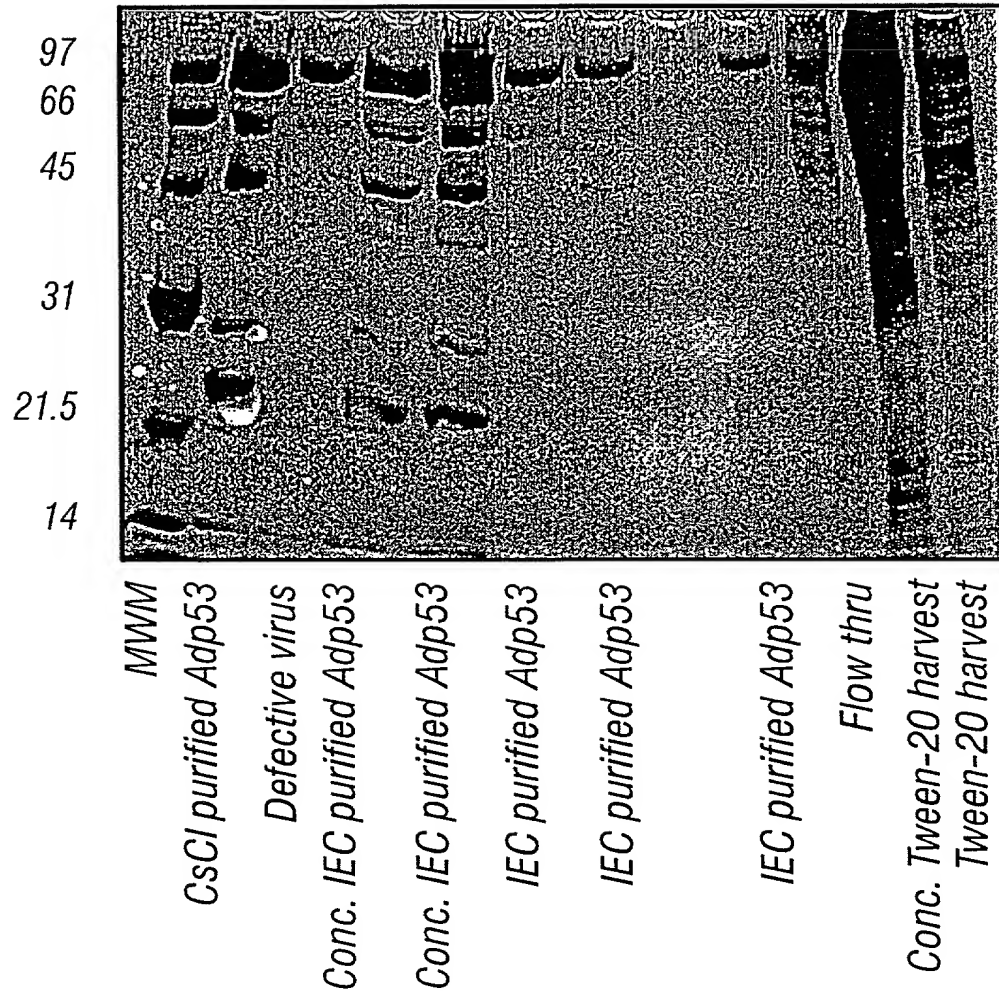
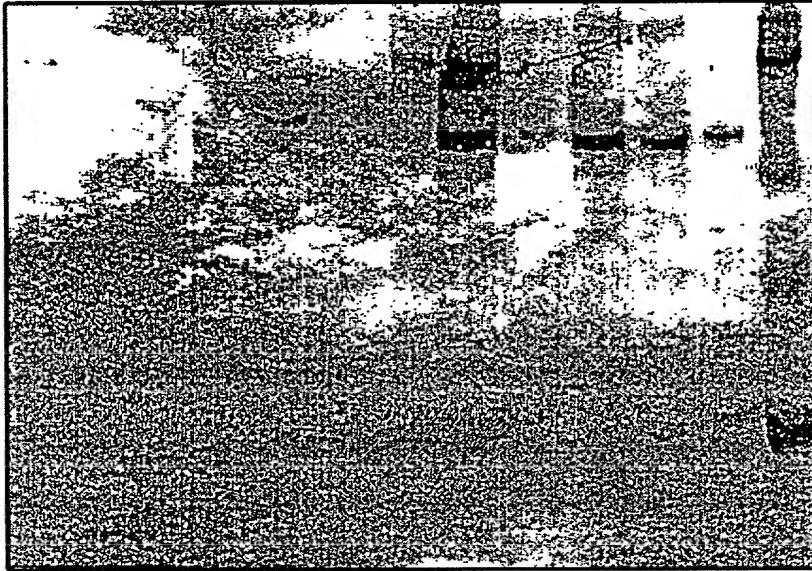


FIG. 19A

IEC purified virus  
 MW marker  
 Blank  
 IEC purified virus  
 Flow through  
 Diluted Benzonase treated  
 virus solution  
 Conc./diafil. virus sol.  
 1% Tween HVST  
 MW marker  
 MW marker



← BSA

FIG. 19B

T02T90" 60908860

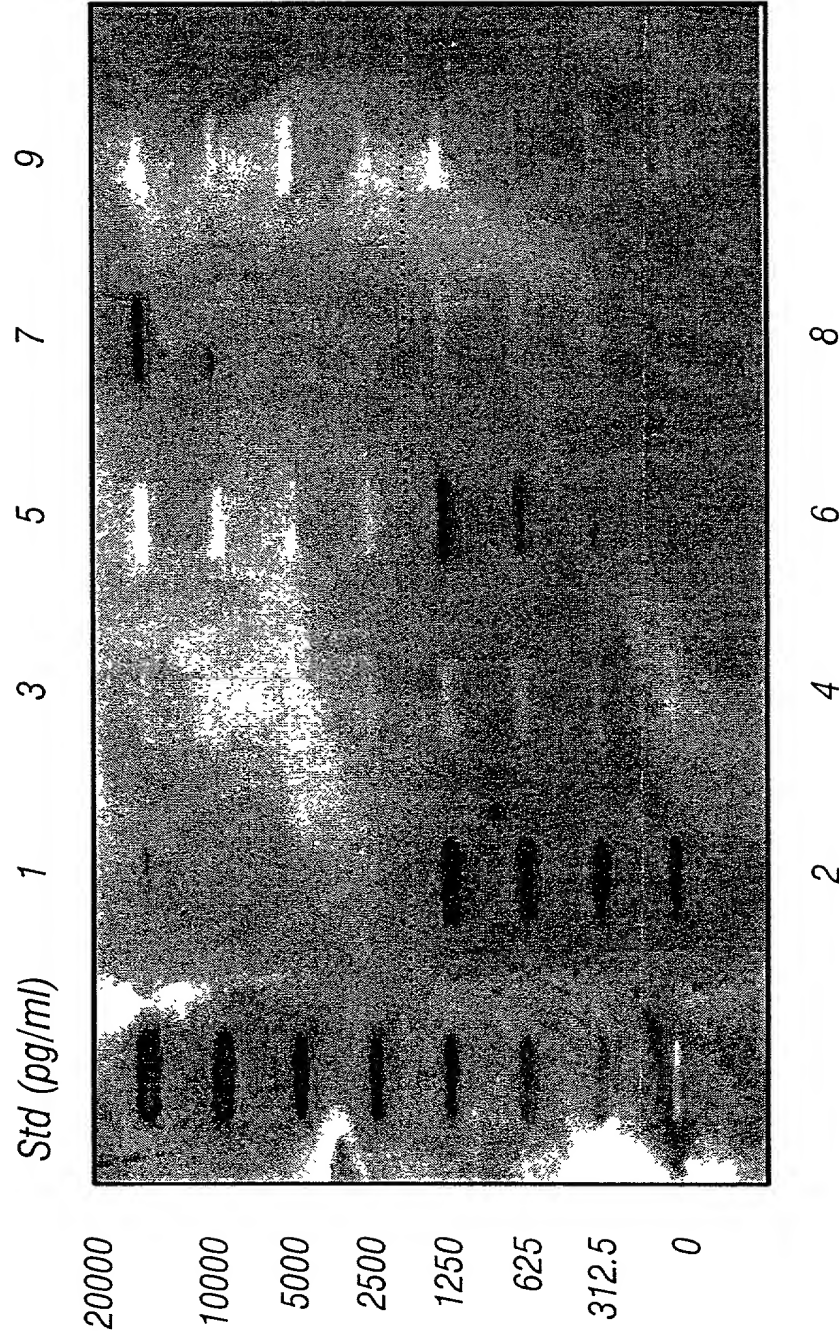


FIG. 19C

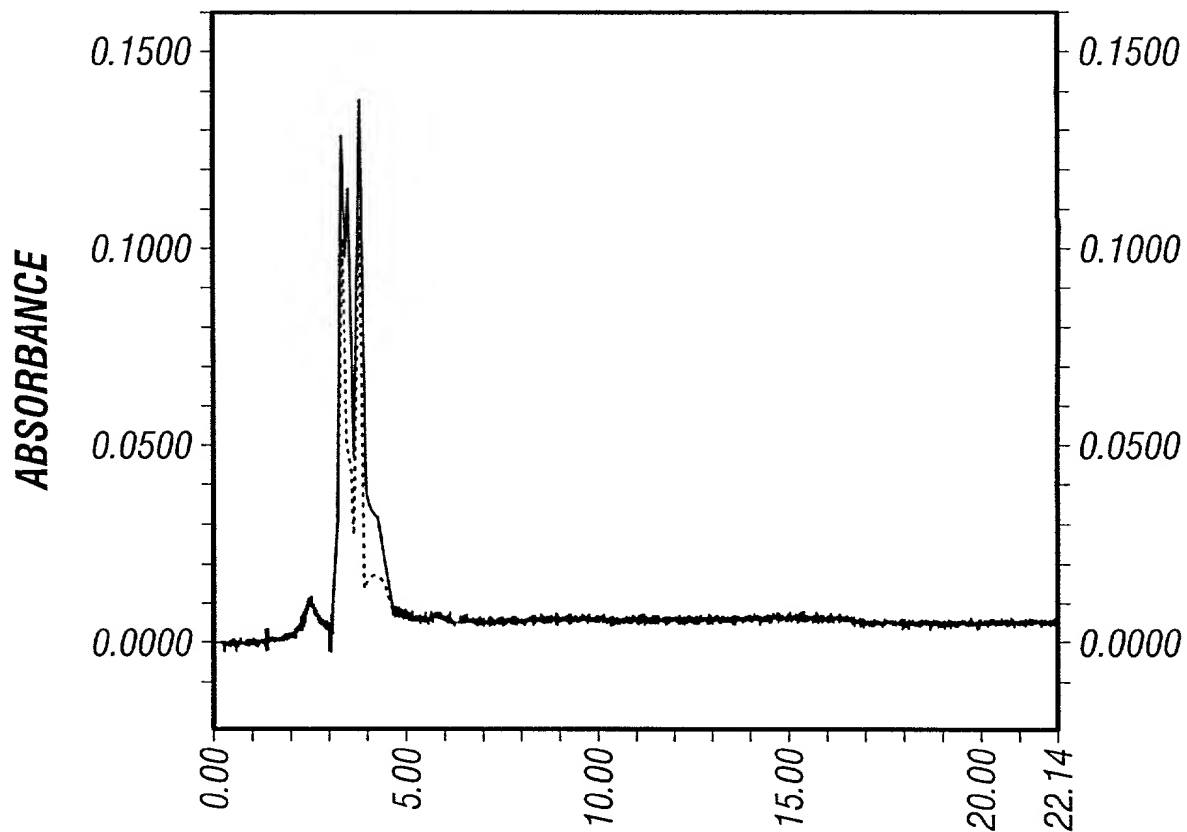


FIG. 20A

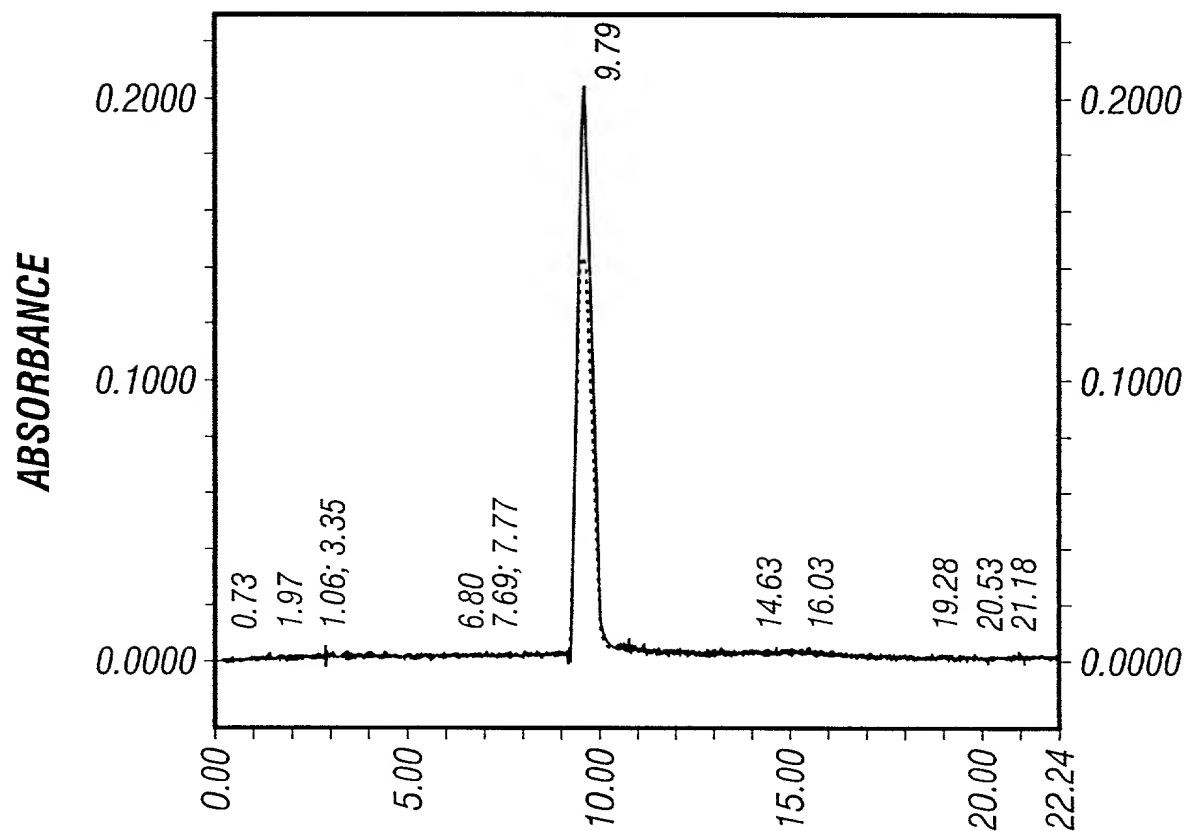


FIG. 20B

27/48

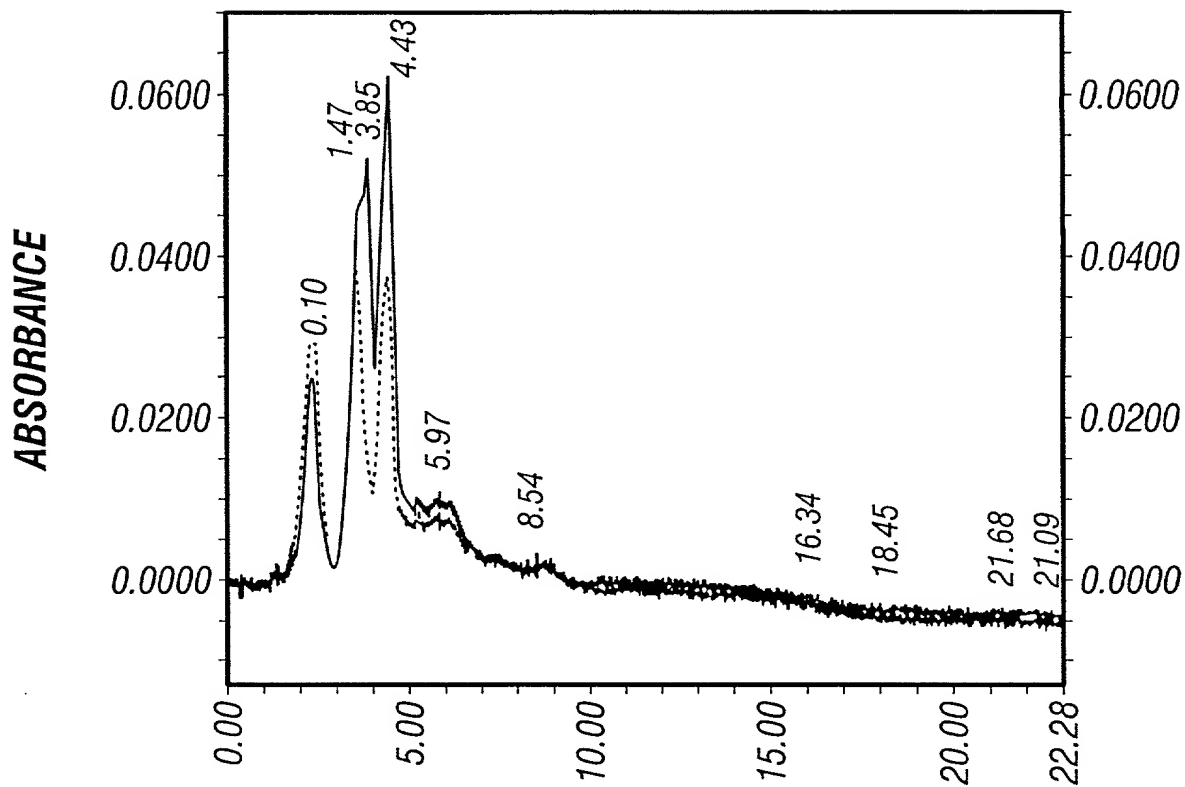


FIG. 20C

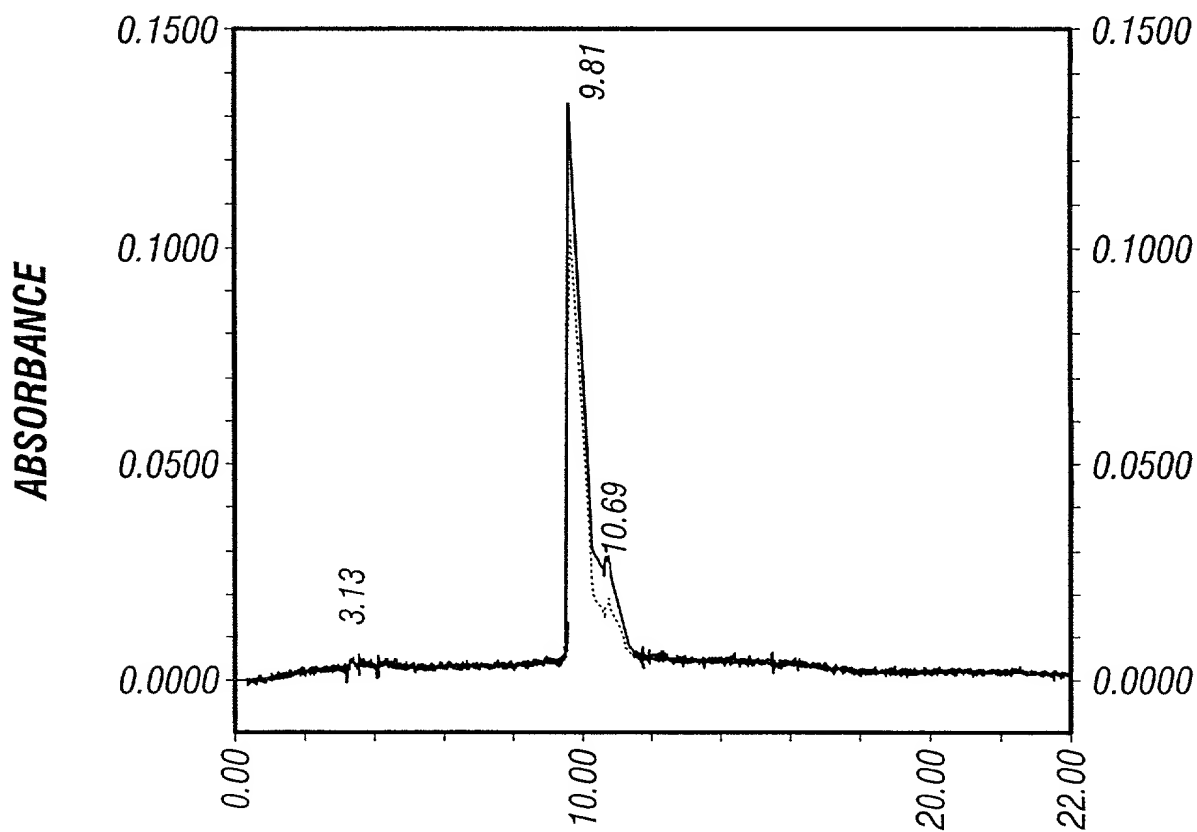


FIG. 20D

28/48

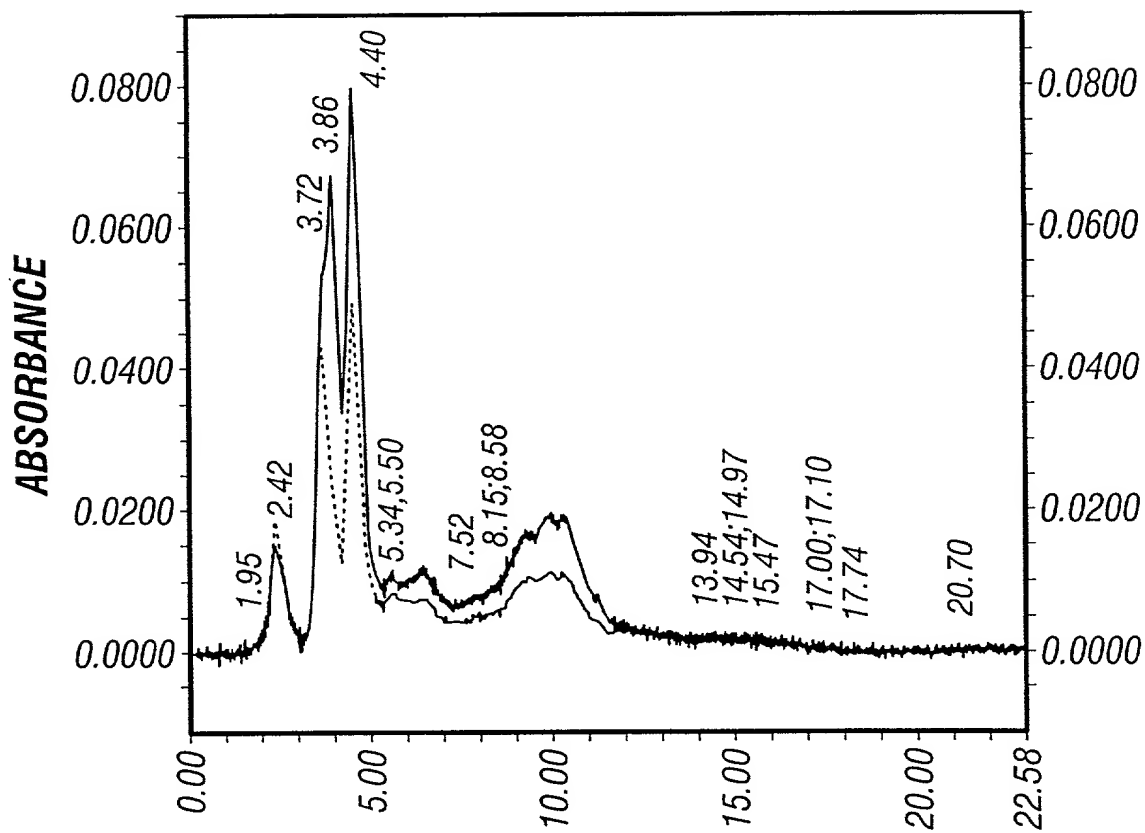


FIG. 20E

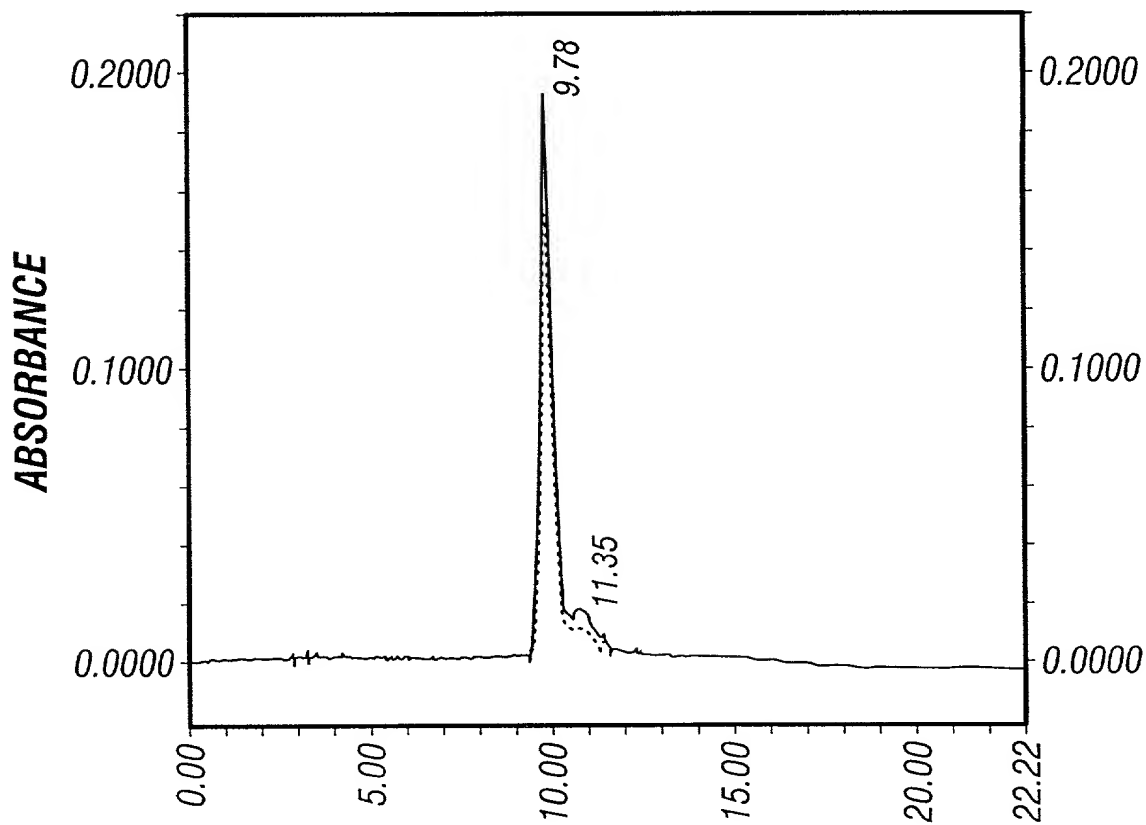
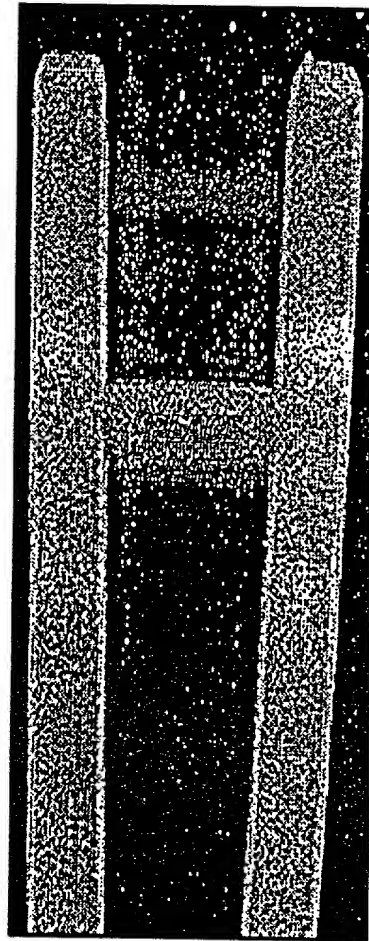
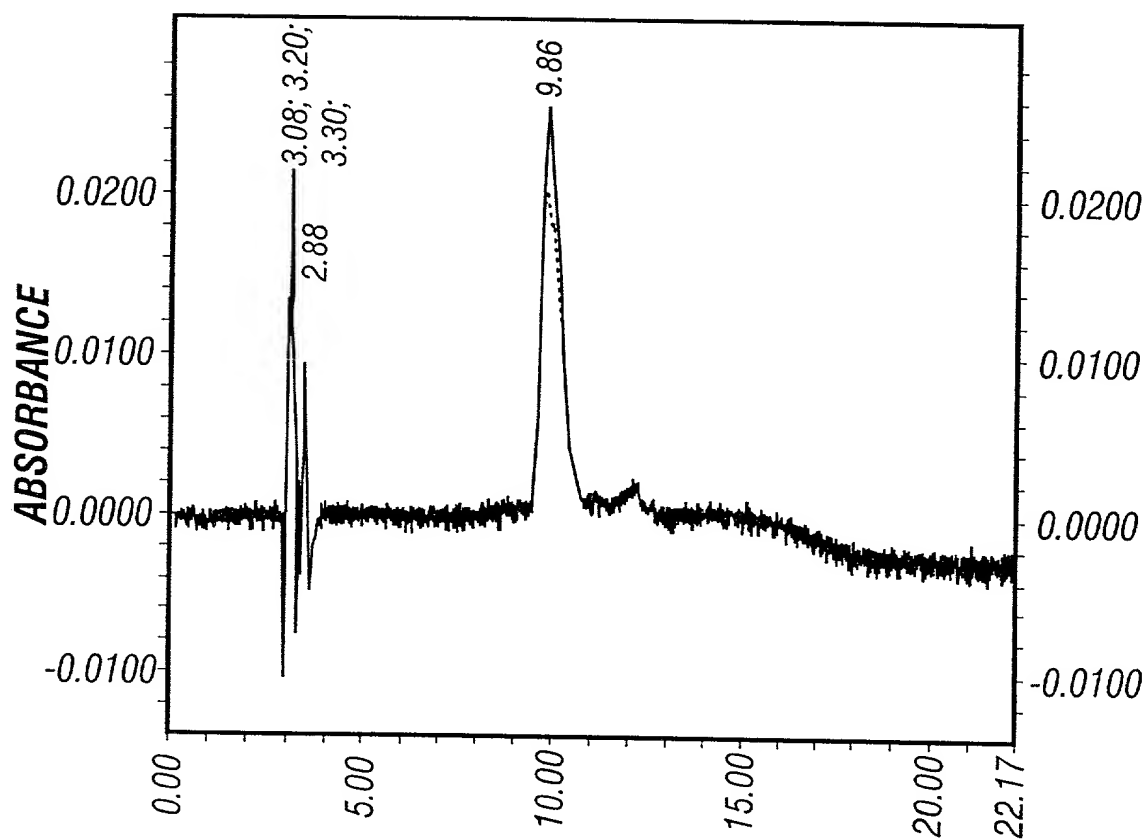
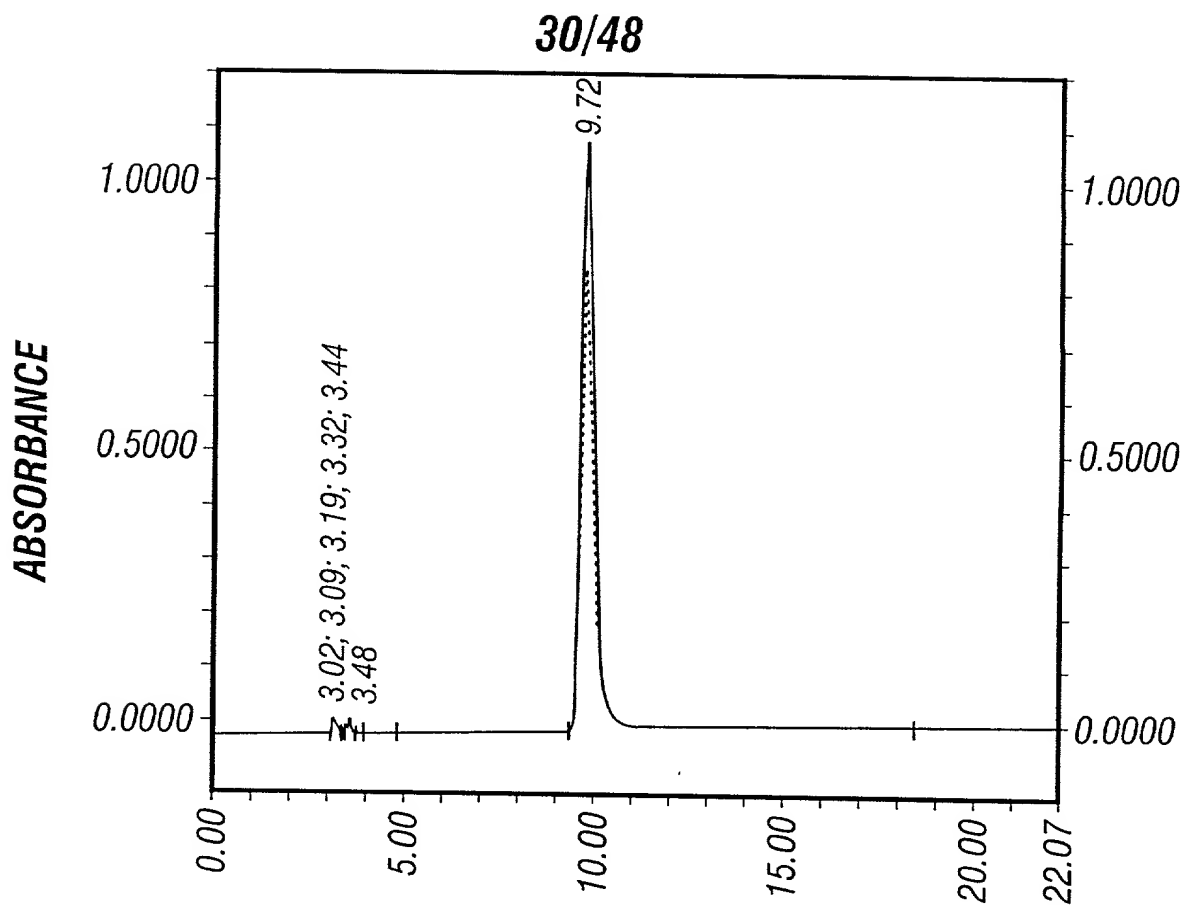


FIG. 20F



**FIG. 21**

102190" 60903860





Cube	(low perfusion rate, keep glucose > 1g/L 1% Tween-20 in buffer A	Titer (PFU/ml)	Vol. (ml)	Yield (PFU)	Recovery %	
					Step	Acc.
Harvest	Clarification and Filtration (0.22 $\mu$ m)					
Virus solution		$2.6 \times 10^9$	1900	$4.9 \times 10^{12}$		
	Conc./diaf. (10-fold conc., diaf. into 1m NaCl buffer A)					
Conc. sup		$2.5 \times 10^{10}$	200	$5 \times 10^{12}$	102%	
	Benzonase treatment (O/N, RT, 100u/ml)					
Treated sup	Diluted with water to conductivity = 22-25 mS/cm					
Diluted virus solution		$7 \times 10^9$	700	$4.9 \times 10^{12}$	98%	100%
purified virus		$1.5 \times 10^{10}$	240	$3.6 \times 10^{12}$	73%	73%
	conc./diaf (5-fold conc.)					
Final purified product		$7 \times 10^{10}$	50	$3.5 \times 10^{12}$	97%	71%

FIG. 23

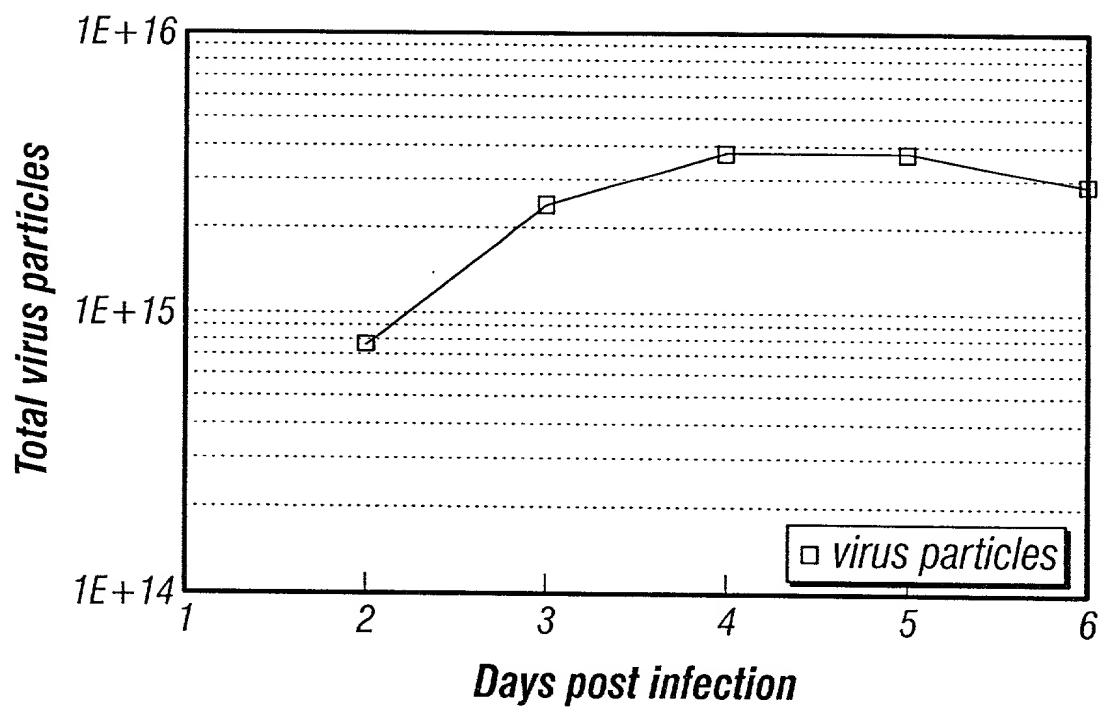


FIG. 24

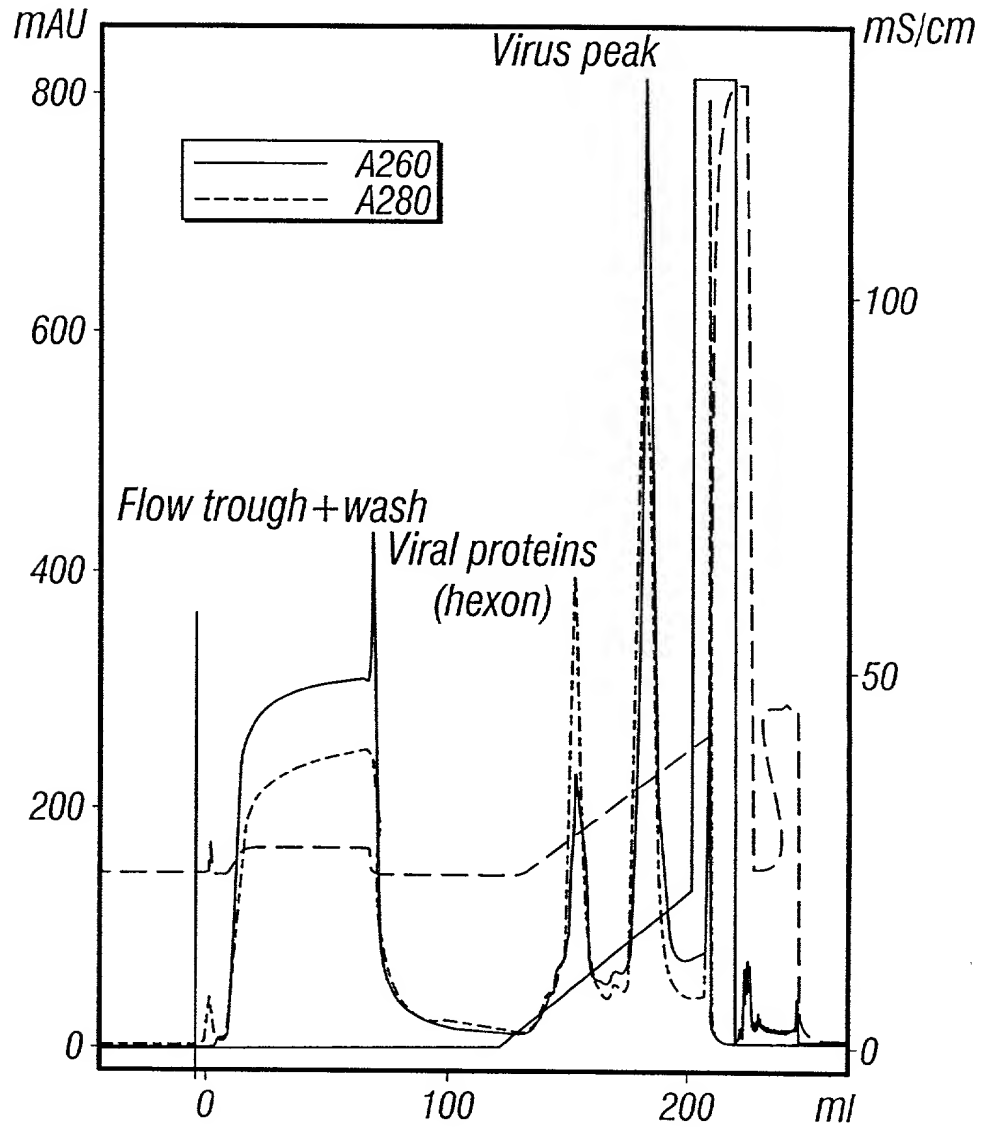


FIG. 25

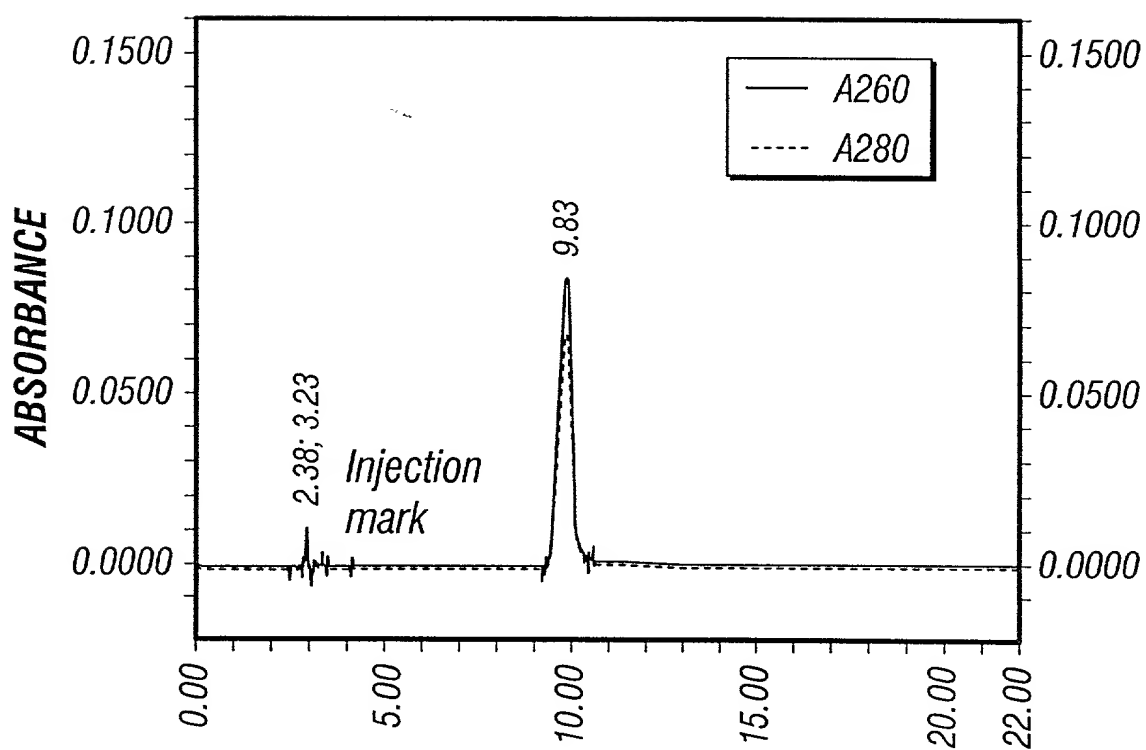


FIG. 26

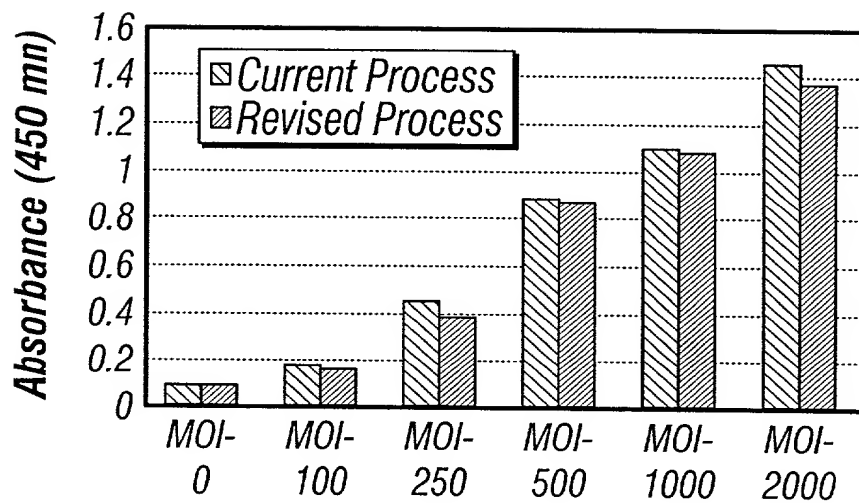


FIG. 27A

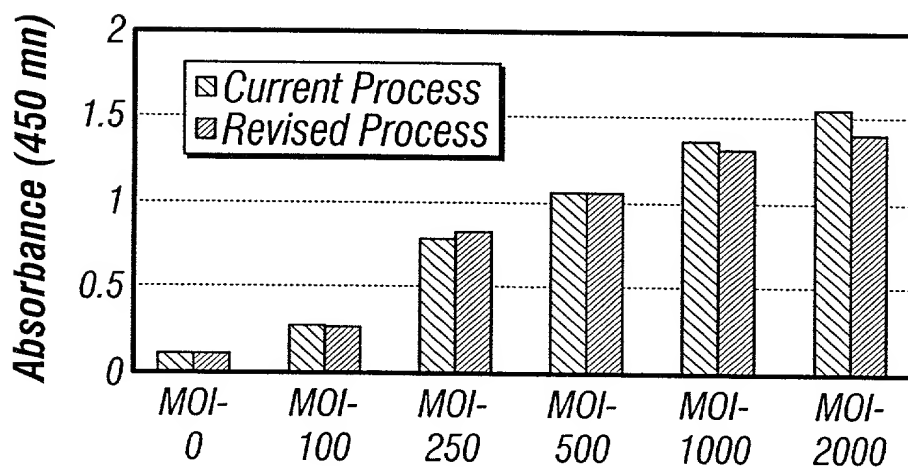


FIG. 27B

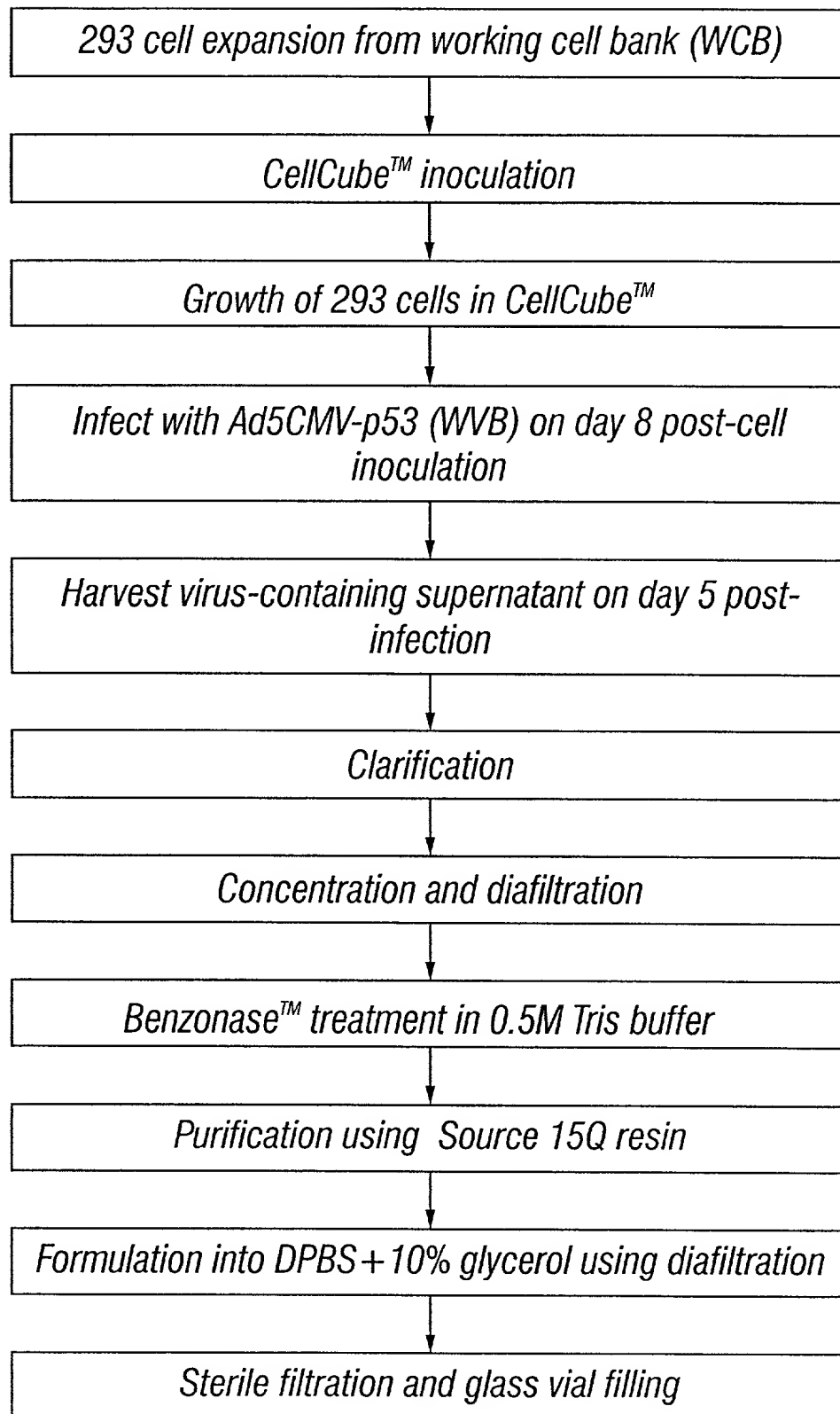


FIG. 28

FIG. 29

Date (Temp.)	PFU x 10 <sup>9</sup> /ml				HPLC viral particles (x10 <sup>10</sup> )/ml				Water Content (W%)			
	SET 10-6	SET 10-7	SET 10-8	SET 10-9	SET 10-6	SET 10-7	SET 10-8	SET 10-9	SET 10-6	SET 10-7	SET 10-8	SET 10-9
4/11/97	5.5	6	5.8	6.5	24.5	24.6	24.9	26.7	2.2	2.5	2.7	3.3
5/15/97 (-20°C)	7.6	7.1	7.5	8.1	22.4	25.6	26.8	28.5	2.2	2.5	2.8	3.3
5/15/97 (4°C)	6.5	6.3	6.5	10	22	23	24	27.5	2.4	2.6	3	3.4
5/15/96 (R.T.)	7.1	7.1	6.7	3.3	14.5	16.5	6.2	4.2	2.7	2.9	3.2	3.5
7/18/97 (-20°C)	6.8	6.4	6.8	7.2	28.7	28.9	28.6	31.2	2.3	2.5	2.8	3.3
7/18/97 (4°C)	6	5.8	7.3	9	25	26.6	27.6	31.1	2.5	2.8	3	3.6
7/18/97 (R.T.)	1.2	0.8	4	1.4	0.9	1.8	0.7	0.7	2.7	2.9	3	3.4
10/22/97 (-20°C)	7.9	7.5	7.9	7.8	25.5	25	25.4	26.2	2.4	2.6	2.8	3.1
10/22/97 (4°C)	6.8	6.8	5.8	8	22	23	24.7	24.2	2.7	2.9	3.2	3.6
10/22/97 (R.T)	<0.01	<0.01	<0.01	<0.01	N.D.	N.D.	N.D.	N.D.	2.7	2.9	3.1	3.4
4/16/98 (-20°C)	6	5.8	7.1	7.2	19.3	20.3	23.5	26.1	2.4	2.6	3	3.4
4/16/98 (4°C)	5.4	7.2	6.1	6.3	21.7	22.8	22.9	24.6	2.9	3.1	3.3	3.8
4/16/98 (R.T.)	0.0003	0.001	0.0007	0.001	N.D.	N.D.	N.D.	N.D.	2.7	2.9	3.1	3.4

N.D.: Not detectable

FIG. 30A-1

## CONTROLS

Date	PFU x 10 <sup>9</sup> /ml				HPLC viral particles (x10 <sup>10</sup> )/ml			
	SET 10-6	SET 10-7	SET 10-8	SET 10-9	SET 10-6	SET 10-7	SET 10-8	SET 10-9
4/11/97	5.5	7	7	7	35.5	35.8	36	36.9

FIG. 30A-2



Date (Temp.)	PFU x 10 <sup>9</sup> /ml				HPLC viral particles (x10 <sup>10</sup> )/ml				Water Content (W%)			
	SET 11-6	SET 11-7	SET 11-8	SET 11-9	SET 11-6	SET 11-7	SET 11-8	SET 11-9	SET 11-6	SET 11-7	SET 11-8	SET 11-9
5/2/97	7	6	6.3	5.8	28.5	28.8	28.4	29.5	2.3	2.7	3.5	4
6/20/97 (-20°C)	6.2	6.6	6.9	6.5	26.3	25	27	27.3	2.2	2.8	3.4	4.6
6/20/97 (4°C)	6.1	6	6.5	6.5	24.1	22.1	25.6	26.6	2.5	2.8	3.5	4.8
6/20/97 (R.T.)	3.3	3	1	<0.1	20.5	17.4	5.2	9.1	2.7	3.1	3.5	4.7
8/18/97 (-20°C)	8	7.2	7.5	7.6	21.6	21.8	25.3	24.9	2.3	2.8	3.7	4.9
8/18/97 (4°C)	8	7.3	8	8	22.7	22.7	24.9	25	2.6	3	3.9	4.2
8/18/97 (R.T.)	<0.1	<0.1	<0.1	<0.1	N.D.	N.D.	0.2	13.1	2.7	3	3.5	4.4
10/22/97 (-20°C)	7.9	7.5	7.9	6.7	21	22	25.1	24	2.4	3	3.9	4.4
10/22/97 (4°C)	6	6.9	6.8	7.3	21.4	22	23.1	23.1	2.6	3	3.3	4.6
10/22/97 (R.T.)	<0.01	<0.01	<0.01	<0.01	N.D.	N.D.	N.D.	9	2.7	2.9	3.9	5
5/8/98 (-20°C)	8.3	7.5	8	8.7	19	18.2	19.9	21.1	2.6	3.1	4	4.6
5/8/98 (4°C)	7	7.1	7.8	6.5	17.3	17.1	18.2	17.8	2.8	3.2	4.1	5.1
5/8/87 (R.T.)	0.00033	0.000065	0.00045	0.000016	N.D.	N.D.	N.D.	N.D.	2.7	2.9	4	4.9

N.D.: Not detectable

FIG. 30B-1

## CONTROLS

		CONTROLS							
Date		PFU x 10 <sup>9</sup> /ml				HPLC viral particles (x10 <sup>10</sup> )/ml			
		SET 11-6	SET 11-7	SET 11-8	SET 11-9	SET 11-6	SET 11-7	SET 11-8	SET 11-9
5/2/97		6.4	6.8	6.5	6.5	37.7	36.7	37.3	36

FIG. 30B-2

Date (Temp.)	PFU x 10 <sup>9</sup> /ml SET 10-6 SET 10-7 SET 10-8 SET 10-9				HPLC viral particles (x10 <sup>10</sup> )/ml SET 10-6 SET 10-7 SET 10-8 SET 10-9				Water Content (W%) SET 10-6 SET 10-7 SET 10-8 SET 10-9			
5/15/97	6.5	5.6	6.1	6	18	18.6	21.9	23.3	0.8	1.1	1.3	1.5
6/20/97 (4 °C)	5.4	5.6	5.5	5.5	14.6	14.9	17.2	16.6	0.8	1.2	1.5	1.6
6/20/97 (R.T.)	4.5	5	5.5	6	10.8	11.8	15	15.4	1.3	1.4	1.6	1.9
8/18/97 (4 °C)	7	6.7	6.8	7	15.3	17.1	17.9	17.7	1.3	1.5	1.5	1.7
8/18/97 (R.T.)	2.4	2.2	4.8	5.8	4.3	7.2	11.7	14.2	1.3	1.6	1.7	2.1
11/20/97 (4 °C)	5.5	5.5	5.3	5.7	16.8	16.8	20.6	20.1	1.1	1.4	1.6	1.9
11/20/97 (R.T.)	0.45	0.9	2.3	3.1	1.5	5.5	7.3	10.7	1.3	1.7	1.8	2.2
5/14/98 (4 °C)	4.9	4.7	5.4	6.5	9.7	11.9	12.6	14.2	1.2	1.6	2.2	1.4
5/14/98 (R.T.)	0.000006	0.000006	0.000004	0.000024	N.D.	N.D.	N.D.	N.D.	1.4	1.6	1.3	2

N.D.: Not detectable

FIG. 31A-1

CONTROLS

Date	PFU x 10 <sup>9</sup> /ml				HPLC viral particles (x10 <sup>10</sup> )/ml			
	SET 10-6	SET 10-7	SET 10-8	SET 10-9	SET 10-6	SET 10-7	SET 10-8	SET 10-9
5/15/97	7	5.6	7	7	31.2	30.6	31.6	31.4

FIG. 31A-2

Date (Temp.)	PFU x 10 <sup>9</sup> /ml				HPLC viral particles (x10 <sup>10</sup> )/ml				Water Content (W%)			
	SET 11-6	SET 11-7	SET 11-8	SET 11-9	SET 11-6	SET 11-7	SET 11-8	SET 11-9	SET 11-6	SET 11-7	SET 11-8	SET 11-9
5/22/97	7.5	6.3	7.3	6.5	17.4	16.6	20.3	24.7	1	1.2	1.6	1.9
6/20/97 (4 °C)	5.5	6.3	6	7.5	14.8	16.1	17.5	21.1	1.2	1.3	1.7	1.8
6/20/97 (R.T.)	5	6	6	7.5	12.6	14.9	17.2	20.3	1.4	1.6	1.9	2
8/18/97 (4 °C)	6.3	6.7	6.8	7.5	15.7	17.2	18.5	22.6	1.2	1.5	1.8	1.9
8/18/97 (R.T.)	3.3	4.5	5.5	7	7.4	10.5	15.8	21.2	1.6	1.7	1.9	2.2
11/20/97 (4 °C)	5.3	5.6	5.3	6.6	17.3	20	22.6	26.3	1.2	1.4	1.9	1.9
11/20/97 (R.T.)	0.8	1.9	3	0.2	3.2	7.9	14.2	1.3	1.6	1.7	2	2.1
5/14/98 (4 °C)	6.7	7.2	6.9	7.6	12.4	13.9	15.5	18.5	1.3	1.6	2	2.2
5/14/98 (R.T.)	0.0013	0.00005	0.00031	0.00045	N.D.	N.D.	N.D.	N.D.	1.6	1.8	1.6	2

N.D.: Not detectable

FIG. 31B-1

CONTROLS

Date	PFU x 10 <sup>9</sup> /ml SET 11-6 SET 11-7 SET 11-8 SET 11-9				HPLC viral particles (x10 <sup>10</sup> )/ml SET 11-6 SET 11-7 SET 11-8 SET 11-9			
5/22/97	8	7.4	8.3	7.6	26.7	27.6	27.5	32.4

FIG. 31B-2

Date (Temp.)	PFU x 10 <sup>9</sup> /ml				HPLC viral particles (x10 <sup>10</sup> )/ml				Water Content (W%)			
	SET 10-6	SET 10-7	SET 10-8	SET 10-9	SET 10-6	SET 10-7	SET 10-8	SET 10-9	SET 10-6	SET 10-7	SET 10-8	SET 10-9
6/13/97	3.4	4.3	4.1	4.2	16	16.5	16.1	18.1	0.8	1.1	1.3	1.4
7/18/97 (4 °C)	6.3	6.3	6	6	17.9	19.5	19.9	20.6	0.9	1.2	1.4	1.6
7/18/97 (R.T.)	4.1	5.5	5	5.5	11.4	15.5	18.2	20.6	1.2	1.4	1.7	1.8
9/16/97 (4 °C)	4.2	5.5	4.5	5.1	15.3	16.1	16.4	17.8	1	1.3	1.5	1.7
9/16/97 (R.T.)	0.7	1.2	5	4	2.9	5	9.5	13	1.3	1.5	1.8	2
12/4/97 (4 °C)	5.5	5.3	5.4	5.9	16.1	16.2	18.1	18.5	1.1	1.4	1.6	1.7
12/4/97 (R.T.)	0.3	0.5	2.5	3.4	N.D.	1.7	4.7	8.8	1.4	1.6	1.8	2
6/29/98 (4 °C)	3.8	5.1	5.3	5.4	10.6	10.8	12	12.9	1.3	1.5	1.8	1.9
6/29/98 (R.T.)	0.00003	0.00006	0.0001	0.0001	N.D.	N.D.	N.D.	N.D.	1.4	1.6	1.7	1.8

N.D.: Not detectable

FIG. 32A-1

## CONTROLS

Date	PFU x 10 <sup>9</sup> /ml				HPLC viral particles (x10 <sup>10</sup> )/ml			
	SET 10-6	SET 10-7	SET 10-8	SET 10-9	SET 10-6	SET 10-7	SET 10-8	SET 10-9
6/13/97	4.7	3.8	5.5	6.2	26	26.2	27.4	27.5

FIG. 32A-2

Date (Temp.)	PFU x 10 <sup>9</sup> /ml					HPLC viral particles (x10 <sup>10</sup> )/ml					Water Content (W%)				
	SET 11-6	SET 11-7	SET 11-8	SET 11-9		SET 11-6	SET 11-7	SET 11-8	SET 11-9		SET 11-6	SET 11-7	SET 11-8	SET 11-9	
6/13/97	3.4	4.2	3.6	4.4		16.1	16.3	18.4	19.3		0.9	1.3	1.8	1.9	
7/18/97 (4 °C)	5.5	6.2	6.5	6.2		18	19.5	23	23.9		1	1.4	1.8	2.1	
7/18/97 (R.T.)	3.7	6	6.7	7.3		13.7	18.7	21.8	22.8		1.3	1.7	2	2.2	
9/16/97 (4 °C)	3.9	4	4.6	6		15.6	17.3	19.5	20.6		1.3	1.5	1.9	2.1	
9/16/97 (R.T.)	0.8	2.2	4	5.3		3.6	6.8	13.8	14.6		1.5	1.9	2.3	2.4	
12/4/97 (4 °C)	4.6	5.3	8	6.1		15.7	18.2	21.4	21.6		1.2	1.6	2.1	2.2	
12/4/97 (R.T.)	0.4	0.6	0.3	<0.01		N.D.	N.D.	1.7	N.D.		1.6	1.8	2.1	2.1	
6/29/98 (4 °C)	4.9	5	5.4	6.4		11.4	14.2	13.7	16		1.5	1.7	2.1	2.6	
6/29/98 (R.T.)	0.0001	0.00015	0.00085	0.0012		N.D.	N.D.	N.D.	N.D.		1.6	1.7	2.2	2.3	

N.D.: Not detectable

FIG. 32B-1

## CONTROLS

Date	PFU x 10 <sup>9</sup> /ml					HPLC viral particles (x10 <sup>10</sup> )/ml				
	SET 11-6	SET 11-7	SET 11-8	SET 11-9		SET 11-6	SET 11-7	SET 11-8	SET 11-9	
6/13/97	4.5	5	4	5		26.5	26.9	26.6	27.1	

FIG. 32B-2

Date (Storage Cond.)	PFU x 10 <sup>9</sup> /ml				HPCL viral particles (x10 <sup>10</sup> )/ml			
	10%-G	5%-s,5%-HSA	5%-S,%-PEG	5%-T,1%-PEG	10%-G	5%-s,5%-HSA	5%-S,%-PEG	5%-T,1%-PEG
8/1/97	5.8	4.7	4.3	4.4	16.9	14.5	16.1	16.7
8/28/97 (4°C, N <sub>2</sub> )	5.8	5.8	6.4	6.3	13.3	14.9	13.8	13.4
8/28/97 (4°C, AIR)	5	5.9	6	5.9	12.9	14.2	12.9	12.9
8/28/97 (R.T., N <sub>2</sub> )	4.4	4.8	5	6	12.6	14.5	13.5	12.9
8/28/97 (R.T., AIR)	4.3	5	5	5.6	12.3	13.7	13	13
10/30/97 (4°C, N <sub>2</sub> )	3.8	4	4.7	3.8	14	15.5	14.7	14.8
10/30/97 (4°C, AIR)	3	4.1	3.7	4.7	12.6	14.9	14.3	14.4
10/30/97 (R.T., N <sub>2</sub> )	1.5	3.4	3.5	3.6	13.8	15.1	14.6	14.4
10/30/97 (R.T., AIR)	1.5	3.6	2.2	3.1	12.7	14.7	14.8	14.4
1/12/98 (4°C, N <sub>2</sub> )	3.2	4.1	3.3	3.4	7.3	11.1	9.5	9.5
1/12/98 (4°C, AIR)	1.5	3.8	3.9	3.4	7.7	10.8	10.2	10
1/12/98 (R.T., N <sub>2</sub> )	0.1	1.4	0.7	0.7	10	10.8	11.1	10.4
1/12/98 (R.T., AIR)	0.4	1.6	1	0.4	9.9	11	10	10.4
4/30/98 (4°C, N <sub>2</sub> )	0.08	4.3	4	5.3	5.1	12.3	12.3	12.1
4/30/98 (4°C, AIR)	1.5	3.6	4.4	4.5	5	11.6	11.8	11.9
4/30/98 (R.T., N <sub>2</sub> )	0.0025	0.23	0.11	0.17	11.1	12.3	12.6	12.5
4/30/98 (R.T., AIR)	0.0015	0.21	0.063	0.007	11	12.4	12.3	11

FIG. 33

Date (Temp.)	PFU x 10 <sup>9</sup> /ml											
	AQF2-1	AQF2-2	AQF2-3	AQF2-4	AQF2-5	AQF2-6	AQF2-7	AQF2-8	AQF2-9	AQF2-10	AQF2-11	AQF2-12
9/25/97	2.8	2.8	2.8	3	2.8	2.8	2.7	2.8	2.7	3.3	3.1	2.7
11/05/97 (4°C)	2.3	3.2	2.4	3.6	2.7	2	3.6	3.8	2.7	3	3.5	2.5
11/05/97 (R.T.)	2.2	0.1	2.4	2.7	2.1	2.1	3.2	2.1	3	3	3.4	2.9
12/12/97 (4°C)	2.2	0.1	2.4	2.7	2.1	2.1	3.2	2.1	3	3	3.4	2.9
01/09/98 (R.T.)	1.2	<0.1	0.2	1.2	0.2	0.1	1.3	1.1	0.2	<0.1	2	1.1
3/27/98 (4°C)	1.8	<0.1	1.9	2	<0.1	1.7	2	<0.1	2.6	2.9	2.6	1.8
3/27/98 (R.T.)	0.6	<0.1	<0.1	0.8	<0.1	<0.1	1	<0.1	<0.1	<0.1	1.1	0.7

FIG. 34A-1

Date (Temp.)	HPLC viral particles (x10 <sup>10</sup> /ml)											
	AQF2-1	AQF2-2	AQF2-3	AQF2-4	AQF2-5	AQF2-6	AQF2-7	AQF2-8	AQF2-9	AQF2-10	AQF2-11	AQF2-12
9/25/97	10.9	9.6	9.7	11.3	10.7	10.6	10.9	10.8	10.7	11.4	11.8	10.7
11/05/97 (4°C)	7.9	7.6	8.7	8.8	8.9	7.5	8.6	9.1	9.2	10.3	11.2	9.6
11/05/97 (R.T.)	8.2	6.6	7.6	8.6	7.7	9.3	9	8	9.3	10.3	11.1	9.6
12/12/97 (4°C)	6.7	1.5	8	6.9	5.2	7.5	7.5	6.1	7.6	8.8	7.3	7.7
12/17/98 (R.T.)	7	1.2	7	7.5	4.1	7.1	7	3	8.2	7.6	8.4	7.5
3/13/98 (4°C)	5.6	N.D.	6.2	6.7	N.D.	6.5	6.8	N.D.	7.1	8	8.9	7.2
3/13/98 (R.T.)	6.2	N.D.	6.5	6.9	N.D.	7.3	6.8	N.D.	6.9	7.8	7.5	7.1

FIG. 34A-2

Excipients	AQF2-1	AQF2-2	AQF2-3	AQF2-4	AQF2-5	AQF2-6	AQF2-7	AQF2-8	AQF2-9	AQF2-10	AQF2-11	AQF2-12
Mannitol (W%)	5	5	5				5	5	5	5	5	
Sucrose (W%)				5	5	5	5	5	5	5	5	10
Glycine (M)	0.25			0.25			0.25				0.25	0.25
Arginine (M)		0.25			0.25			0.25			0.25	
Urea (W%)			1			1			1		1	
Peg (W%)										1	1	

FIG. 34B



<i>Date (Temp.)</i>	<i>PFU x 10<sup>9</sup></i>				<i>HPLC viral particles(x 10<sup>10</sup>/ml)</i>			
	<i>F10-7</i>	<i>F10-8</i>	<i>F11-7</i>	<i>F11-8</i>	<i>F10-7</i>	<i>F10-8</i>	<i>F11-7</i>	<i>F11-8</i>
10/3/97	2.2	3.3	2.1	2.8	12.1	12	11.8	12
11/6/97 (-20°C)	3.4	4	2.8	3.4	10.6	10.5	10.1	10.3
11/6/97 (4°C)	3.5	3.6	4.3	2.8	10	9.7	9.9	10.3
1/15/98 (-20°C)	3.8	4.8	3.2	3.7	7.3	7.4	7.7	8
1/15/98 (4°C)	3.5	3.1	2.9	3.1	7.5	7.4	7.6	7.5

FIG. 35-1

<i>Excipients</i>	<i>F10-7</i>	<i>F10-8</i>	<i>F11-7</i>	<i>F11-8</i>
<i>Mannitol (W%)</i>	6	6	5	5
<i>Sucrose (W%)</i>	7	8	7	8
<i>HSA (W%)</i>	0.5	0.5	0.5	0.5
<i>Glycerol (W%)</i>	1	1	1	1
<i>MgCl<sub>2</sub> (mM)</i>	1	1	1	1

FIG. 35-2

Date (Temp.)	PFU x 10 <sup>9</sup>						
	AQF4-1	AQF4-2	AQF4-3	AQF4-4	AQF4-5	AQF4-6	AQF4-7
1/13/98	3	2.5	3.6	3.4	2.7	3.1	3.4
2/11/98 (4°C)	2.5	3.2	3.3	2.9	2.6	2.9	2.6
2/11/98 (R.T.)	1.8	2.7	1.6	3.6	2.6	1.6	1.7
4/10/98 (4°C)	2.2	2	2.6	3	2.4	1.9	2.2
4/10/98 (R.T.)	0.4	0.4	0.3	0.5	0.4	<0.1	1.1
7/24/98 (4°C)	2.4	2.8	2.6	3.5	1.9	2.2	2.6
7/24/98 (R.T.)	0.002	0.005	0.006	0.005	0.005	0.005	0.001

FIG. 36-1

Date (Temp.)	HPCL Intergrated Area						
	AQF4-1	AQF4-2	AQF4-3	AQF4-4	AQF4-5	AQF4-6	AQF4-7
1/13/98	8.7	10.9	11.5	11.1	9.5	9.7	11.3
2/16/98 (4°C)	9.1	9.3	9.2	9.5	8.2	8.4	9.6
2/16/98 (R.T.)	6.8	9	9.5	9	8.7	8.4	9.3
4/10/98 (4°C)	7.1	9.2	9.6	9.6	8.9	9.1	9.9
4/10/98 (R.T.)	7.5	9.5	10.1	9.7	8.9	8.9	9.5
7/24/98 (4°C)	8.1	9.9	11.1	10.3	9.2	7.4	9.3
7/24/98 (R.T.)	7.3	3	10.7	8.9	10.4	10.45	3.5

FIG. 36-2

Excipients	AQF4-1	AQF4-2	AQF4-3	AQF4-4	AQF4-5	AQF4-6	AQF4-7
Mannitol (W%)	5	5	5	5	5	5	5
Sucrose (W%)	5	5	5	5	5	5	5
Tween 80 (W%)		0.02	0.1	0.5			
Chap (W%)					0.02	0.1	0.5

FIG. 36-3

DECLARATION

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or the below named inventors are the original, first and joint inventors (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled **AN IMPROVED METHOD FOR THE PRODUCTION AND PURIFICATION OF ADENOVIRAL VECTORS**, the Specification of which:

- ☐ is attached hereto.  
☒ was filed on **December 1, 1998** as Application Serial No. **09/203,078**.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims.

I acknowledge the duty to disclose to the Patent and Trademark Office all information known to me to be material to patentability of the subject matter claimed in this application, as "materiality" is defined in Title 37, Code of Federal Regulations, § 1.56.

I hereby claim priority benefits under Title 35, United States Code, § 119 of any foreign application(s) for patent, United States provisional application(s), or inventor's certificate listed below and have also identified below any foreign application for patent, United States provisional application, or inventor's certificate having a filing date before that of the application on which priority is claimed:

PRIORITY APPLICATION(S)			Priority Claimed
60/031,329	US	November 20, 1996	Yes
(Number)	(Country)	(Date Filed)	Yes/No

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose all information known to me to be material to patentability of the subject matter claimed in this application, as "materiality" is defined in Title 37, Code of Federal Regulations, § 1.56, which become available between the filing date of the prior application and the national or PCT international filing date of this application:

08/975,519

November 20, 1997

Pending

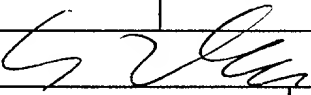
(Application Serial No.)


(Filing Date)

(Status)

I hereby direct that all correspondence and telephone calls be addressed to David L. Parker, Arnold White & Durkee, P.O. Box 4433, Houston, Texas 77210, (512) 418-3000.

I HEREBY DECLARE THAT ALL STATEMENTS MADE OF MY OWN KNOWLEDGE ARE TRUE AND THAT ALL STATEMENTS MADE ON INFORMATION AND BELIEF ARE BELIEVED TO BE TRUE; AND FURTHER THAT THESE STATEMENTS WERE MADE WITH THE KNOWLEDGE THAT WILLFUL FALSE STATEMENTS AND THE LIKE SO MADE ARE PUNISHABLE BY FINE OR IMPRISONMENT, OR BOTH, UNDER SECTION 1001 OF TITLE 18 OF THE UNITED STATES CODE AND THAT SUCH WILLFUL FALSE STATEMENTS MAY JEOPARDIZE THE VALIDITY OF THE APPLICATION OR ANY PATENT ISSUED THEREON.

Inventor's Full Name:	Shuyuan	Zhang
Inventor's Signature:		
Country of Citizenship:	China	Date: 1/4/99
Residence Address: (street, number, city, state, and/or country)	3027 Orchard Gate, Sugar Land TX 77479	
Post Office Address: (if different from above)		

Inventor's Full Name:	Capucine	Thwin
Inventor's Signature:		
Country of Citizenship:	U.S.A	Date: 1/4/99
Residence Address: (street, number, city, state, and/or country)	9018 HERTS ROAD SPRING TX 77379	
Post Office Address: (if different from above)		

Inventor's Full Name:	Zheng		Wu
Inventor's Signature:	<i>Zheng Wu</i>		
Country of Citizenship:	P.R.C.	Date:	1/4/99
Residence Address: (street, number, city, state, and/or country)	2930 Cotton Stock Dr. Sugar Land, TX 77479		
Post Office Address: (if different from above)			

Inventor's Full Name:	Toohyon		Cho
Inventor's Signature:			
Country of Citizenship:		Date:	
Residence Address: (street, number, city, state, and/or country)			
Post Office Address: (if different from above)			

Inventor's Full Name:	Shawn		Gallagher
Inventor's Signature:	<i>Shawn L. Gallagher</i>		
Country of Citizenship:	U.S.A.	Date:	1/4/99
Residence Address: (street, number, city, state, and/or country)	1730 Shoreline Drive Missouri City, TX 77459		
Post Office Address: (if different from above)			

**PATENT**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of:  
Shuyuan Zhang  
Capucine Thwin  
Zheng Wu  
Toohyon Cho  
Shawn Gallagher

Group Art Unit: 1623

Examiner: Unknown

Atty. Dkt. No.: INGN:081/HYL

Serial No.: 09/203,078

Filed: December 1, 1998

For: AN IMPROVED METHOD FOR THE  
PRODUCTION AND PURIFICATION OF  
ADENOVIRAL VECTORS

**CERTIFICATE OF MAILING  
37 C.F.R. § 1.8**

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as First Class Mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, on the date below:

April 13, 1999  
Date

Steven L. Highlander

**DECLARATION OF MS. ONITA CHEYNE  
UNDER 37 C.F.R. § 1.47**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

I, Onita Cheyne, declare that:

1. I am a U.S. citizen, residing at 10931 Crown Colony Drive, Austin, Texas. I am employed as a prosecution paralegal with the law firm of Arnold, White & Durkee, Austin, Texas.

2. Dr. Toohyon Cho is a former employee of Introgen Therapeutics, Inc., the entity which owns all intellectual property rights of the present invention. Dr. Cho is a co-inventor of the above-referenced patent application and owes a duty of assignment by virtue of his employment agreement at Introgen.

3. In the filing of a previous patent application, Serial No.: 08/975,519, of which the present application is continuation-in-part, Dr. Cho was informed of Inventors' Oath and Declaration papers that required his signature. Dr. Cho was forwarded a complete copy of the application papers, including the specification, claims, abstract, drawings, Oath and Declaration, via Federal Express to his last known address: 874 Yorkchester, #102, Houston, Texas 77079. Dr. Cho was contacted further by telephone and indicated his unwillingness to sign the Oath and Declaration papers which were sent to him with the patent application. Dr. Cho was contacted a second time by telephone and he again refused to sign the inventors' Oath and Declaration (copies attached).

4. In the normal course of business, on March 31, 1999, I forwarded a complete copy of the application papers, including the specification, claims, abstract, drawings, Oath and Declaration, to Dr. Cho via Federal Express to his last known address: 874 Yorkchester, #102, Houston, Texas 77079. On April 2, 1999, I received a telephone call from Federal Express stating that Dr. Cho could not be reached at his last known address. The enclosed documents were returned via Federal Express on April 5, 1999, as undeliverable.

5. I hereby declare that all statements made herein of my knowledge are true and that all statements made herein on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the U.S. Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

4-13-99

DATE

Onita Cheyne

Onita Cheyne

09880609-064201  
FOI 90-60908860



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:  
Shuyuan Zhang et al.

Serial No.: 09/203,078

Filed: December 1, 1998

For: METHOD FOR THE PRODUCTION AND  
PURIFICATION OF ADENOVIRAL  
VECTORS

Group Art Unit: 1623

Examiner: K. Cresy

Atty. Dkt. No.: INRP:081/SLH

CERTIFICATE OF FACSIMILE TRANSMISSION  
37 C.F.R. 1.8

I hereby certify that this correspondence is being sent via facsimile  
(703) 308-6916 to Examiner Karen Cresy with the U.S. Patent and  
Trademark Office, Washington, D.C. 20231, on the date below:

February 13, 2001  
Date

Steven L. Highlander

**REVOCATION OF POWER OF ATTORNEY AND  
ELECTION UNDER 37 C.F.R. §§ 3.71 AND 3.73  
AND CHANGE OF CORRESPONDENCE ADDRESS**

Commissioner for Patents  
Washington, D.C. 20231

Sir:

The undersigned, being in the above-identified application by virtue of an assignment recorded at Reel No. 9924 and Frame No. 0455 in the United States Patent and Trademark Office as set forth below, hereby elects, under 37 C.F.R. § 3.71, to prosecute the application to the exclusion of the inventors.

The Assignee hereby revokes any previous Powers of Attorney and appoints:

Louis T. Pirkey, Reg. No. 22,393; David D. Bahler, Reg. No. 30,932; David L. Parker, Reg. No. 32,165; Richard J. Groos, Reg. No. 32,231; Stephen D. Dellett, Reg. No. 32,564; William G. Barber, Reg. No. 33,154; Michael S. Metteauer, Reg. No. 34,875; Mark B. Wilson, Reg. No. 37,259; Steven L. Highlander, Reg. No. 37,642; John J. Bruckner, Reg. No. 35,816; Erik R. Nordstrom, Reg. No.

39,792; Teresa J. Schultz, Reg. No. 40,526; Stephen P. Meleen, Reg. No. 40,724; Robert E. Hanson, Reg. No. 42,628; Michael C. Barrett, Reg. No. 44,523; Mark T. Garrett, Reg. No. 44,699; Gina N. Shishima, Reg. No. 45,104; Stephen M. Hash, Reg. No. 45,490; Debra L. Dennett, Reg. No. 46,370; and Matthew Bellinger, Reg. No. 46,547;

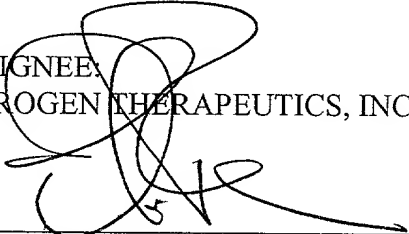
each an attorney or agent of the firm of FULBRIGHT & JAWORSKI L.L.P., as its attorney or agent for so long as they remain with such firm, with full power of substitution and revocation, to prosecute the application, to make alterations and amendments therein, to transact all business in the Patent and Trademark Office in connection therewith, and to receive any Letters Patent, and for one year after issuance of such Letters Patent to file any request for a certificate of correction that may be deemed appropriate.

Pursuant to 37 C.F.R. § 3.73, the undersigned has reviewed the evidentiary documents, specifically the Assignment to INTROGEN THERAPEUTICS, INC., referenced below, and certifies that to the best of my knowledge and belief, title remains in the name of the Assignee.

Please direct all communications as follows:

Steven L. Highlander  
FULBRIGHT & JAWORSKI L.L.P.  
600 Congress Avenue, Suite 2400  
Austin, Texas 78701  
512/536-3184

ASSIGNEE:  
INTROGEN THERAPEUTICS, INC.

By:   
Name: David L. Parker  
Title: Vice President of Intellectual  
Property

Date: February 12, 2001

ASSIGNMENT:

- ☐ Concurrently filed  
☒ Previously recorded  
Date: 4/16/99  
Reel: 9924  
Frames: 0455